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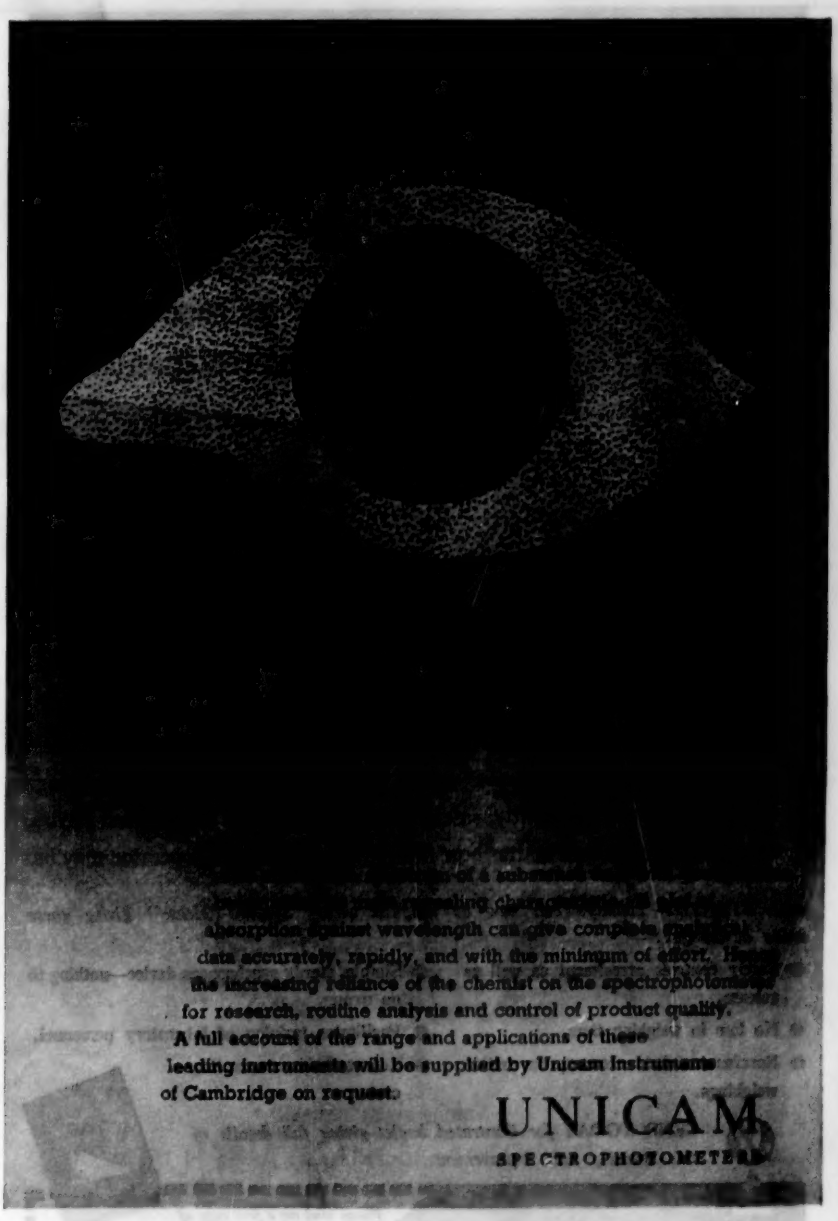
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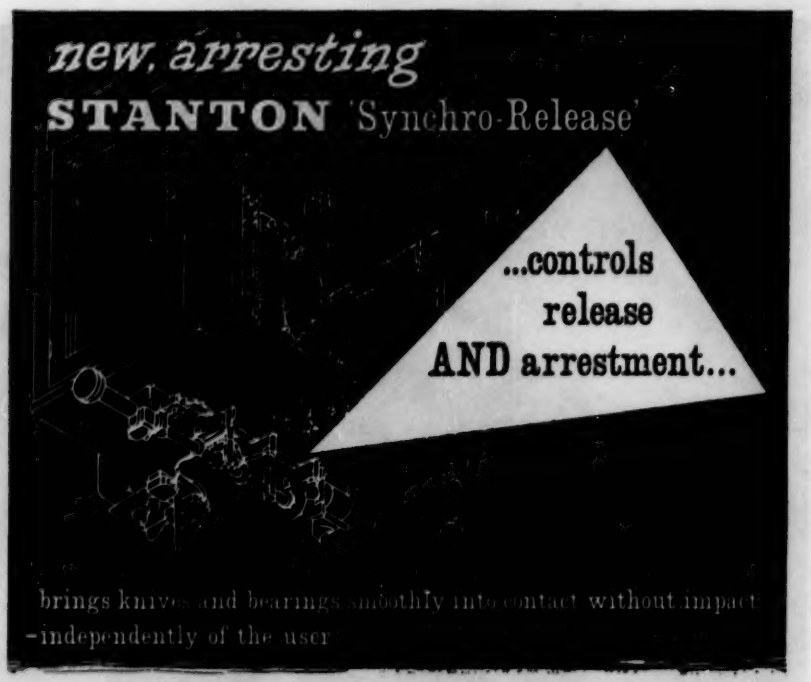
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The Polysaccharides of Chara *(a Fresh-water Alga). Part I. The Isolation and Study of* Chara *Cellulose.*

By El S. Amin.

[Reprint Order No. 5482.]

Chara cellulose gives, on hydrolysis, only D-glucose. The preparation of cellobiose octa-acetate indicates a β-1 : 4-linkage, confirmed by the optical activity of the methylated polysaccharide which on hydrolysis gave 2 : 3 : 6-tri- and 2 : 3-di-*O*-methyl-D-glucose. The results indicate that *Chara* cellulose is similar to cotton cellulose.

Few of the carbohydrates occurring in fresh-water algae have been investigated, in contrast to those of marine algae (Whistler and Smart, "Polysaccharide Chemistry," Academic Press, New York, 1953; Hough, Jones, and Wadman, *J.*, 1952, 3393).

Chara (class Chlorophyceae; order Charales; family Characeae), freshly harvested in December, 1952, from Lake Idku, Egypt, was extracted successively with alcohol (to remove fats and chlorophyll), water, methanol, cold dilute sodium carbonate, and hot sodium hydroxide. The remaining insoluble product was neutral, and soluble in Schweizer's reagent, and gave a blue colour with iodine after treatment with zinc chloride. Hydrolysis gave 85% of D-glucose, the identity of which was confirmed by paper chromatography and osazone formation. Cellobiose octa-acetate was prepared, proving the β-1 : 4-linkage. Oxidation with periodate indicated a chain length of 180 glucose units. *Chara* cellulose was then exhaustively methylated with methyl sulphate and sodium hydroxide in an atmosphere of nitrogen. The specific rotation of the methylated product was similar to that of methylated cotton cellulose, thus supporting the β-1 : 4-linkage, and its hydrolysis products were mainly 2 : 3 : 6-tri-*O*-methyl-D-glucose (90%) with 4% of 2 : 3-di-*O*-methyl-D-glucose. The absence of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose suggests a chain length of not less than 100 glucose units. The presence of the small amount of di-*O*-methyl-D-glucose may be due to demethylation during the hydrolysis (cf. Hirst, Hough, and Jones, *J.*, 1949, 928; Barker, Bourne, and Wilkinson, *J.*, 1950, 3027) or to incomplete methylation. The above results support those of Hough, Jones, and Wadman (*loc. cit.*) and of Percival and Ross (*J.*, 1949, 3041) concerning the relation of algal cellulose to cotton cellulose.

Experimental

Evaporations were done at 50° under reduced pressure unless otherwise stated. Chromatography was carried out on Whatman No. 1 filter paper by the descending method (Partridge, *Biochem. J.*, 1948, **42**, 238) with *n*-butanol–ethanol–water (5 : 1 : 4 v/v). Sugars were detected on the paper chromatogram with *p*-anisidine hydrochloride. All treatments with alkali were done in a nitrogen atmosphere.

Preparation of Chara *Cellulose.*—The alga (10 kg.) was a tangled mass of long green filaments (2 mm. in diameter). It was cleaned and washed in water. After being drained from excess of moisture the filaments were steeped in ethyl alcohol (6 + 6 + 7 l.) for 3 days. The insoluble product was dried in a vacuum at room temperature, ground to a fine pale green powder (yield, 1 kg.), and extracted with hot water (4 l.), methyl alcohol (4 l.; 6 hr.), 1·5% sodium carbonate solution (4 l.; 3 days; removed a trace of polysaccharide), 4% sodium hydroxide solution at 100° (4 l.; 3 hr.; removed 0·2% of polysaccharide) and 25% sodium hydroxide at 100° (4 l.; 3 hr.; removed 0·04% of polysaccharide). The extracts were clarified on the centrifuge (3500 r.p.m.) and then poured into ethyl alcohol (5 parts) with vigorous stirring. An appreciable precipitate appeared from the 4% sodium hydroxide extract and was proved to contain carbohydrate. The residual insoluble fluffy material was washed with water and 2N-acetic acid and extracted with ethyl alcohol and then acetone (Soxhlet) for 12 hr. The insoluble material was dried to constant wt. (yield, 400 g., 4% of the fresh alga) and gave sulphated ash 2·5%, N 0·1%.

Hydrolysis of Chara *Cellulose.*—A portion (0·2 g.) was hydrolysed with 72% sulphuric acid according to Monier-Williams's directions (*J.*, 1921, **119**, 803), giving 85% of D-glucose (cf. 86%

for cotton cellulose), determined by Somogyi's method (*J. Biol. Chem.*, 1933, **100**, 695) and by polarimetry. Paper chromatography showed only glucose (R_G 0·09). An osazone was prepared in pale yellow needles of the same shape as glucosazone and having m. p. and mixed m. p. 205°.

Chain Length of Chara *Cellulose.*—A portion (80 mg.) in each of five bottles was oxidised with potassium periodate (Brown *et al.*, *Nature*, 1945, **156**, 785). The amount of formic acid corresponds to a chain length of 180 glucose units (cf. 200 units for cotton cellulose).

Cellobiose Octa-acetate.—This was prepared by Hibbert and Barsha's method (*Canad. J. Res.*, 1934, **10**, 178). Recrystallised from ethyl alcohol, it had m. p. and mixed m. p. 221°, $[\alpha]_D^{25}$ +39° (*c*, 0·5 in $CHCl_3$).

Methylated Chara *Cellulose.*—The cellulose (12 g.) was methylated eight times with methyl sulphate and 30% sodium hydroxide solution by the method of Haworth, Montonna, and Peat (*J.*, 1939, 1899) (yield, 9·2 g.) (Found: OMe, 42·5; sulphated ash, 0·4%); $[\alpha]_D^{25}$ −15·2° (*c*, 1·8 in $CHCl_3$).

A portion (560 mg.) was hydrolysed by the method of Hough, Jones, and Wadman (*loc. cit.*) (yield, 520 mg.). Paper chromatography gave spots corresponding to 2 : 3 : 6-tri- (R_G 0·83) and 2 : 3-di-*O*-methyl-D-glucose (R_G 0·57). The two methyl sugars were estimated quantitatively by alkaline hypoiodite (Hirst, Hough, and Jones, *loc. cit.*), a phosphate buffer being used according to Chanda *et al.* (*J.*, 1950, 1289), giving 90% of tri- and 4% of di-*O*-methyl-D-glucose.

A portion (150 mg.) of the hydrolysate was separated on the paper chromatogram and the methyl sugars were extracted (Hough, Jones, and Wadman, *loc. cit.*). The first fraction gave 2 : 3 : 6-tri-*O*-methyl-D-glucose, m. p. and mixed m. p. 120°, $[\alpha]_D^{22}$ +69° (*c*, 1·5 in H_2O) (Found: OMe, 39·5. Calc. for $C_9H_{18}O_6$: 41·9%).

ALEXANDRIA UNIVERSITY, EGYPT. [*Received, June 21st*, 1954.]

The Polysaccharides of Chara *(a Fresh-water Alga). Part II.* The Isolation and Study of* Chara *Hemicellulose.*

By EL S. AMIN.

[Reprint Order No. 5483.]

Chara hemicellulose (0·2%), on hydrolysis, gave D-glucose (85%), D-xylose (10·5%), L-arabinose (2·5%), and uronic acid (2%; probably D-glucuronic acid). Methylation of the hemicellulose or of its acetyl derivative and subsequent hydrolysis gave 2 : 3 : 4 : 6-tetra- (3·4%), 2 : 3 : 6-tri-, (90·5%), and 2 : 3-di-*O*-methyl-D-glucose (3·5%), and 2 : 3-di-*O*-methyl-D-xylose (2%).

Chara hemicellulose was extracted with dilute sodium hydroxide solution after primary extraction with hot water and dilute sodium carbonate (to remove carbohydrates other than hemicellulose). It was purified by several precipitations from alcohol, formation of an insoluble copper complex, and dialysis. The product was soluble in water, had a high positive optical rotation, and gave a purple colour with iodine changing to blue. It is hydrolysed by saliva. Hydrolysis by mineral acid and paper chromatography disclosed mainly glucose, with a little xylose and arabinose, identification being as glucosazone and di-*O*-benzylidene-D-xylose dimethyl acetal. The uronic acid (2%) was not galacturonic acid as it did not yield mucic acid. Further evidence was afforded by methylation of either the acetyl derivative or the hemicellulose with methyl sulphate and sodium hydroxide, followed by methyl iodide and silver oxide. The methylated material, after fractionation, had a high positive optical rotation. Examination of the fission products on the paper chromatogram showed mainly 2 : 3 : 6-tri- and small quantities of 2 : 3 : 4 : 6-tetra- and 2 : 4-di-*O*-methyl-D-glucose, and 2 : 3-di-*O*-methyl-D-xylose. The methylpentose arose from the contaminating xylan. Crystalline 2 : 3 : 6-tri-*O*-methyl-D-glucose and the crystalline aniline derivative of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose were isolated.

* Part I, preceding paper.

Experimental

Chromatography, alkali extractions, and evaporations were done as in the preceding paper.

Preparation of Chara *Hemicellulose.*—*Chara* powder (2 kg.; cf. preceding paper) was extracted with 1·5% sodium carbonate solution (2 × 5 l.) at room temperature for 2 days, and with boiling water (20 × 20 l.) for 4 hr. until the extracts on evaporation and hydrolysis were non-reducing to Fehling's solution. The residue (850 g.) was dried and extracted at 100° with 4% sodium hydroxide solution (2 × 15 l.) for 3 hr. It was filtered through muslin, the filtrate centrifuged, the extract acidified with glacial acetic acid with ice-cooling and then centrifuged, and the clear centrifugate poured into 96% ethyl alcohol (5 parts) with stirring. The amorphous precipitate was separated in the centrifuge, then further purified by dissolution in ammonia and precipitation as the copper complex with 25% copper chloride solution. The copper complex was washed with water, then alcohol, followed by ethanolic hydrogen chloride (5%) until the washings were copper-free and finally with ethanol until chloride-free. The amorphous product was dried at 50° under reduced pressure (yield, 40 g., 0·2%); it had $[\alpha]_D^{28}$ +128·5° (*c*, 1 in N-NaOH), and contained sulphated ash 4%, N, 0·3%.

The finely powdered material (15 g.) was repeatedly dissolved in water and precipitated with acetone. The product was washed with alcohol and ether and dried to constant weight. Since analysis showed a high ash content (3·2%) and nitrogen content (0·3%), it was further purified by dialysis. The substance was dissolved in 0·01N-hydrochloric acid and dialysed for 48 hr. against water. After precipitation with acetone (5 parts), the hemicellulose was filtered off, redissolved, and reprecipitated with alcohol. The precipitate was washed with alcohol and ether and dried (yield, 8 g.).

This *Chara* hemicellulose was an amorphous material, dissolving slowly in hot water to form a viscous solution. It was insoluble in organic solvents, had $[\alpha]_D^{28}$ +130·5° (*c*, 0·6 in N-NaOH) and $\eta_{sp.}^{25}$ 0·047 (*c*, 0·2 in N-NaOH), and gave sulphated ash 0·01% and N 0·01%. It gave with iodine a purple colour, changing to blue. After the material had been treated with saliva, the iodine colour reaction was negative.

Hydrolysis of Chara *Hemicellulose.*—A portion (360 mg.) was heated with N-sulphuric acid (25 c.c.) at 100° for 12 hr. in a sealed tube. The acid, in which was suspended a small amount of flocculent material (9 mg.), was neutralised with barium carbonate and filtered, and the filtrate de-ionised with a mixture of Amberlite resin IR-120 and IR-400. It was then concentrated to a syrup (320 mg.). Examination of a portion on the paper chromatogram gave spots corresponding to glucose (R_G 0·09), arabinose (R_G 0·12), and xylose (R_G 0·15). A portion (102 mg.) of the hydrolysate was separated on a paper chromatogram; after being dried, the appropriate parts of the paper were extracted with hot methanol and the carbohydrates determined by Somogyi's copper reagent, giving glucose (85%), xylose (10·5%), and arabinose (2·5%). The amount (2%) of uronic acid was determined by Le Fèvre and Tollens's method (*Ber.*, 1907, **40**, 4513). The uronic acid was not galacturonic acid since with nitric acid it did not give mucic acid.

Another portion of the hydrolysate (150 mg.) was fractionated on the paper chromatogram and extracted with methanol. The first fraction had $[\alpha]_D^{26}$ +54·2° (equil.; *c*, 0·6 in H_2O). It gave an osazone, m. p. 205° undepressed on admixture with authentic glucosazone. The second fraction gave a dibenzylidene dimethyl acetal (Breddy-Jones, *J.*, 1945, 738), m. p. 211° undepressed on admixture with the D-xylose derivative.

Acetylation of Chara *Hemicellulose.*—A portion (4 g.) of the dry powdered polysaccharide was warmed with pyridine (100 c.c.) for 2 hr. at 70°. It was cooled and kept overnight at room temperature. Acetic anhydride (40 c.c.) was added dropwise during 0·5 hr. The mixture was incubated at 52° for 3 days. The clear solution was diluted with acetic acid (100 c.c.) and poured into ethyl alcohol (2 l.) with stirring. The white amorphous product was isolated by means of a centrifuge, washed with alcohol and ether, and dried (yield, 3·2 g.). Reacetylation was carried out as above, giving a product of $[\alpha]_D^{24}$ +128° (*c*, 0·8 in $CHCl_3$).

Methylation of Chara *Hemicellulose.*—(*a*) Hemicellulose (6 g.) was suspended in water (40 c.c.) and allowed to swell for 2 hr. The air was then displaced by nitrogen, a gentle stream of the gas being maintained throughout. The flask was cooled to 10° and 30% (w/w) sodium hydroxide (80 c.c.) was added with vigorous stirring. After 2 hr. methyl sulphate (40 c.c.) was added dropwise during 8 hr. Stirring was continued overnight, and the reaction was completed by heating at 50° for an hour. The mixture was cooled and treated with 30% sodium hydroxide solution (100 c.c.), followed by methyl sulphate (50 c.c.) as before. It was then neutralised with 0·5N-sulphuric acid and dialysed for 2 days. The methylation was repeated six times in

presence of acetone (80 c.c.) at room temperature without cooling. The acidified mixture was extracted with chloroform, the solvent removed from the extract, and the product dissolved in 1 : 4 aqueous acetone. It was twice methylated with methyl sulphate and sodium hydroxide as above, giving a product of $[\alpha]_D^{25}$ +130° (*c*, 1 in $CHCl_3$) (Found : OMe, 38; sulphated ash, 0·2%). The methylated substance was treated with methyl iodide (80 c.c.) and silver oxide (40 g.) under reflux for 6 hr. and after the reaction was complete, had $[\alpha]_D^{25}$ +145° (*c*, 0·8 in $CHCl_3$) (Found : OMe, 41%).

(*b*) The acetylated hemicellulose was stirred with acetone (150 c.c.) and methylated with methyl sulphate (70 c.c.) and sodium hydroxide solution (140 c.c.) as above. After eight methylations the product was purified by precipitation from light petroleum (b. p. 40—60°), giving a white amorphous substance (3·6 g.). It was remethylated with methyl iodide and silver oxide, giving a product of $[\alpha]_D^{25}$ +150° (*c*, 1 in $CHCl_3$) (Found : OMe, 41·6%). The methylated product was fractionated by successive extractions under reflux with mixtures of light petroleum (b. p. 60—80°) and chloroform in the ratios 95 : 5, 90 : 10, and 85 : 15. The main product (80%) was found in the last solvent mixture; it had $[\alpha]_D^{25}$ +149° (*c*, 0·8 in $CHCl_3$) (Found : OMe, 41·5%).

Fission of Methylated Chara *Hemicellulose.*—(*a*) A portion (0·7 g.) was heated with methanolic hydrogen chloride (3%) in a sealed tube for 7 hr. at 100°. The product was neutralised with cold ethereal diazomethane, concentrated at normal temperature, and refluxed with 4% hydrochloric acid for 7 hr., then neutralised with silver carbonate, filtered, de-ionised with a mixture of Amberlite resins IR-120 and IR-400, and evaporated to a syrup (560 mg.). Paper chromatography indicated the presence of 2 : 3 : 4 : 6-tetra- (R_G 1·0), 2 : 3 : 6-tri- (R_G 0·83), and 2 : 3-di-*O*-methyl-D-glucose (R_G 0·57), and 2 : 3-di-*O*-methyl-D-xylose (R_G 0·74). The methyl sugars, determined by the alkaline hypoiodite micro-method of Hirst, Hough, and Jones (*loc. cit.*), were 2 : 3 : 4 : 6-tetra- (3·4%), 2 : 3 : 6-tri- (90·5%), and 2 : 3-di-*O*-methyl-D-glucose (3·5%), and 2 : 3-di-*O*-methyl-D-xylose (2%). Another portion of the hydrolysate was separated on the paper chromatogram, the methyl sugars located, and sections of the remainder of the chromatogram extracted with hot methanol, giving on evaporation 2 : 3 : 6-tri-*O*-methyl-D-glucose, m. p. and mixed m. p. 120° (from ether), $[\alpha]_D^{22}$ +66° (*c*, 1·8 in H_2O) (Found : OMe, 40·1. Calc. for $C_9H_{18}O_6$: OMe, 41·9%).

(*b*) The methylated polysaccharide (0·6 g.) was heated in methanolic 2% hydrochloric acid (50 c.c.) under reflux for 7 hr. The fully methylated sugar (27 mg.) was isolated from the mixture by Brown and Jones's quantitative procedure (*J.*, 1947, 1344). It was hydrolysed in N-sulphuric acid for 6 hr. to syrupy 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose (14 mg.), $[\alpha]_D^{20}$ +84° (*c*, 0·8 in H_2O). It gave an aniline derivative, m. p. and mixed m. p. 132° [from light petroleum (b. p. 60—80°)].

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The Effect of Molecular Structure of Paraffins on Relative Chlorination Rates.

By G. Chambers and A. R. Ubbelohde.

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Comparisons between homologues and isomers show that within the reaction range investigated the overall rate of monochlorination increases with increasing chain length and decreases with chain branching. This influence of molecular structure on monochlorination is analogous to its influence on rates of oxidation.

Relative reaction rates of chlorine atoms with primary, secondary, and tertiary hydrogen atoms in paraffins are discussed in the light of previous publications and of new experimental findings. For normal paraffins, the reactivity of secondary relative to primary hydrogen appears to decrease as the chain lengthens. An important factor may be the flexibility of the paraffins and their relative ability to assume crumpled forms.

A change observed in the surface activity of Pyrex glass during chlorination is interpreted as due to the replacement of hydrophilic groups in the surface by hydrophobic organosilicon groups.

In the physical chemistry of paraffins, a key problem is to interpret the marked influence of molecular structure on reactivity, notwithstanding the presence of much the same C–H and C–C bonds in all cases. This influence of molecular structure is particularly marked in oxidation, which may, however, involve some rather special reaction steps (Small and Ubbelohde, *J. Appl. Chem.*, 1953, **3**, 193). Reactions of the paraffins which involve simpler steps can be of value in elucidating the controlling factors. For this reason, chlorination in the gas phase has been re-investigated.

The thermal and photochemical chlorination of paraffins is believed to proceed by a chain mechanism (Pease and Walz, *J. Amer. Chem. Soc.*, 1931, **53**, 3728; Yuster and Reyerson, *J. Phys. Chem.*, 1935, **39**, 859; Vaughan and Rust, *J. Org. Chem.*, 1940, **5**, 449) involving the steps:

$$(1)\ Cl_2 \xrightarrow[\text{light}]{\text{Heat or}} Cl\cdot + Cl\cdot;\ \Delta H = +57 \text{ kcal./mole.}$$

$$(2)\ Cl\cdot + RH \longrightarrow R\cdot + HCl;\ \Delta H = 0 \text{ to } -13 \text{ kcal./mole.}$$

$$(3)\ R\cdot + Cl_2 \longrightarrow RCl + Cl\cdot;\ \Delta H = -21 \text{ to } -27 \text{ kcal./mole.}$$

The approximate heats of reaction indicated above are based on D(Cl–Cl) = 57·1 kcal., D(H–Cl) = 102·1 kcal., and the values of D(R–H) and D(R–Cl) quoted by Lane, Linnett, and Oswin (*Proc. Roy. Soc.*, 1953, *A*, **216**, 361). Since stage (2) is probably rate-determining, the effect of molecular structure on relative rates of chlorination is likely to depend mainly on local bond energies and on steric factors.

In the present work, the reactivities of a number of isomeric and homologous C_5—C_8 paraffins towards chlorine have been compared. The results show that the order of reactivity is similar to that found in oxidation, although the effects of molecular structure are much less pronounced.

It has been suggested (Ubbelohde and McCoubrey, *Discuss. Faraday Soc.*, 1951, **10**, 94) that the ability of flexible molecules to assume crumpled configurations may be important for hydrocarbon reactivity. Further evidence of this has now been obtained by analysis of the monochlorination products of *n*-hexane; the reactivity of the secondary relative to the primary hydrogen atoms appears to be appreciably less than has been reported (Hass, McBee, and Weber, *Ind. Eng. Chem.*, 1936, **28**, 333) for chlorination of the lower paraffins.

Experimental

Purification of Materials.—Cylinder nitrogen was freed from oxygen by passage through a large steel tube containing copper turnings at 550°. Subsequently, moisture was removed

in a "Birlec Lectro Dryer." The surface of the copper in the deoxygenator was kept in an active condition by frequent regeneration with hydrogen.

Commercial chlorine was purified by three trap-to-trap distillations in nitrogen. In each, generous first and last fractions were blown to waste. The pure liquid was stored at −78° with a slow stream of nitrogen passing through it.

The normal paraffins were freed from olefins by prolonged treatment with 20% oleum. This process also assisted removal of branched-chain isomers, which are more readily sulphonated. The *iso*-paraffins were freed from olefins by successive washings with small volumes of concentrated sulphuric acid until coloration of the acid layer no longer occurred. Subsequent treatment of all the hydrocarbons involved washing with 30% potassium hydroxide solution, then water, partial drying (Na_2SO_4), final drying by refluxing with sodium wire, and fractionation, under nitrogen, through a 60-cm. column, packed with porcelain rings. Refractive indices and b. p. ranges of the materials finally accepted are as shown in Table 1.

TABLE 1.

	n-Pentane	*n*-Hexane	*n*-Heptane	2 : 3-Dimethyl-butane	2 : 2 : 4-Trimethyl-pentane
Boiling range/76 cm.	35—36°	67·5—68·5°	97·5—98·5°	58·2—58·5°	98·5—99·0°
n_D^{20}	1·3586	1·3786	1·3913	1·3756	1·3925

Apparatus.—A flow system was used. The central feature was a Pyrex reaction tube similar to that used in recent investigations of oxidation reactions in this laboratory (Small and Ubbelohde, *J.*, 1953, 637) except that the mixing chamber did not contain Pyrex chips and glass wool, which were found to have an unreproducible effect on chlorination rates. Methods of obtaining reproducible reaction surfaces were also different (see below). For the photochemical experiments, illumination was provided by four 200-watt bulbs, directly above the reaction tube and under an efficient metallic reflector. As it was necessary to run the photochlorinations at >80°, the heating effect of the lamps was supplemented by electrical heating from resistance wire wound directly on to the reaction vessel, at a uniform spacing of 1 cm. between turns. Reaction temperatures were recorded by a thermometer, placed in an axial pocket in the gas flow. In the thermal experiments, the reaction tube was snugly surrounded by an electrically heated steel furnace, from which light was completely excluded.

Chlorine was carried into the reaction vessel by a metered stream of nitrogen, which passed through two saturators in series containing the liquid, held at −78° by an intimate mixture of solid carbon dioxide and alcohol. In calibrating tests, the total amount of chlorine carried through the reaction vessel in a known time was determined by titration of the iodine liberated when the exit gases were passed into potassium iodide solution. Comparison of the analytical results with values calculated from nitrogen flow rates, the vapour pressure of chlorine at −78° (67·5 mm.), and barometric pressure readings indicated that the saturating devices had an efficiency of better than 99%.

Hydrocarbons were carried into the reaction zone as vapours in the same way. For these liquids the carburettors were placed in a thermostat, at temperatures such as to give a partial pressure of 400 mm. for each of the paraffins used. In order to prevent condensation, the parts of the carburettors above the level of the thermostat liquid, and the Pyrex tube connecting the carburettors to the reaction vessel, were electrically heated. Blank experiments with each of the hydrocarbons showed that at least 98% of the calculated volume could be recovered in cooled traps beyond the reaction zone. Flow rates (in c.c./min., calc. at S.T.P.) in photochemical and thermal experiments were: hydrocarbon vapour, 202; chlorine, 22·1; nitrogen, 408. These rates gave a constant contact time of 50·8 secs. with the cross section of reaction vessel used.

Precautions were taken to ensure that chlorination occurred only in the vapour phase and under the controlled conditions in the reaction tube. Thus, light was excluded from all parts of the system beyond the furnace exit; portions of the collecting train were electrically heated to 150°, which was insufficient to cause thermal chlorination, but sufficient to prevent separation of a liquid phase which might act catalytically in the presence of free chlorine. Immediately before each series of experiments, the reactants were freed from dissolved oxygen by passing nitrogen through the carburettors for 30 min. The chlorine was blown to waste, but the hydrocarbon stream was used to sweep out the reaction tube. At the end of each series of experiments, the reaction vessel was again swept out with nitrogen in order to remove products and reactants. When more exhaustive cleaning of the reaction vessel was desired,

it was washed with alcoholic potassium hydroxide, water, a mixture of nitric and sulphuric acids at 100°, and abundant distilled water, and dried at 200° with a slow stream of nitrogen passing through it (see p. 289).

Collection and Analysis of Products.—When it was sufficient to determine only the chlorine consumed in a particular reaction, the effluent gases were passed through bubblers containing potassium iodide solution. Chlorine which escaped reaction was determined by titration with sodium thiosulphate. The hydrogen chloride formed was determined by addition of excess of potassium iodate, followed by further titration with thiosulphate.

When it was desired to recover organic products, the gases leaving the reaction vessel were freed from chlorine and hydrogen chloride by passing them through a scrubber containing saturated sodium carbonate solution. Usually some organic material collected on the surface of the scrubbing solution, and the remainder was condensed in two traps, cooled in solid carbon dioxide and alcohol. The mixture of unchanged hydrocarbon and alkyl chlorides was separated from the aqueous material, washed twice with water, dried (Na_2SO_4), and fractionally distilled. In most cases the object was to determine the extent to which monochlorides had undergone further chlorination, and therefore the only separation attempted was that of monochlorides from hydrocarbon and polychlorides. The products resulting from the chlorination of *n*-hexane under various conditions were analysed in more detail by methods described below.

Detailed Analysis of the Chlorination Products of n-*Hexane.*—Large volumes of *n*-hexane were chlorinated in a number of experiments. The resulting products contained unchanged hexane (*ca.* 90%), the three monochlorides, and small amounts of polychlorides. It was desired to determine accurately the respective amounts of primary and secondary monochlorides in each mixture.

Preliminary experiments showed that distillation at atmospheric pressure, or prolonged refluxing at reduced pressure, resulted in slight, but probably autocatalytic, decomposition of the chlorides with evolution of hydrogen chloride. This was most undesirable, because of the complicating effect of dissolved hydrogen chloride on the method of analysis to be described. Isolation of the monochlorides was therefore carried out under mild conditions and as rapidly as was consistent with efficient separation. In order to prevent excessive local heating, the boiler was immersed in an oil-bath. The bulk of the unchanged hexane was removed by fractionation at 200 mm. through a column (20 × 2 cm.) packed with glass beads. The fractionation was completed, at 35 mm., by using an efficient column (35 × 1 cm., 15—17 plates) packed with $\frac{1}{8}$″ glass helices, and operated at a reflux ratio of 15 : 1. The combined monochlorides were collected in the temperature range 35—42°/35 mm. Throughout these fractionations, the boiler contained a small amount of anhydrous sodium carbonate, which was intended to remove hydrogen chloride. Qualitative tests on the recovered solid showed that only a trace of inorganic chloride was formed. The distillate also was free from hydrogen chloride.

Part of each mixture of monochlorides, separated as described above, was analysed by a further fractionation, at atmospheric pressure, the 35-cm. column being used at a reflux ratio of 20 : 1. A fairly satisfactory separation of 1-chlorohexane (b. p. 135—136°) from a mixture of the secondary chlorides (2-, b. p. 125—126°, and 3-chlorohexane, b. p. 123—124°) was obtained, but slight decomposition of the chlorides occurred. Reduced-pressure fractionation

TABLE 2. *Rate constants for reaction* $C_6H_{13}Cl + KI \longrightarrow KCl + C_6H_{13}I$ *in anhydrous acetone at* 60°.

$k = 1/[t(a - b)] \log b(a - x)/a(b - x)$; k in hr.$^{-1}$ mole l.$^{-1}$.

a = original concn. of RCl; b = original concn. of KI; x = KI reacting in t hr (all in mole/l.).

RCl	1-Chlorohexane	2-Chlorohexane	3-Chlorohexane
10^3k	127·4 (±3·7) [1]	8·2 (±0·3) [2]	4·4 (±0·2)

[1] Cf. 10^3k = 125 (Conant, Kirner, and Hussey, *J. Amer. Chem. Soc.*, 1925, **47**, 476).
[2] Cf. 10^3k = 7·5 (*idem*, *ibid.*).

eliminated decomposition but gave a less satisfactory separation. Hence, the fractionation results were used only as confirmation of an independent method of analysis, modified from that described by Hass and Weber (*Ind. Eng. Chem. Anal.*, 1935, **7**, 231) for mixtures derived from *iso*pentane. Analysis was based on the reaction of the monochlorides with potassium iodide in anhydrous acetone. Rate constants at 60° were determined for each of the pure monochlorides (Table 2). The primary chloride reacted much more rapidly than either of the secondary chlorides. Rate constants for mixtures were a linear function of composition

(Fig. 1). From Fig. 1 the respective amounts of primary and secondary chlorides in a mixture of unknown composition can be determined by measurement of the velocity constant. Since the two secondary chlorides do not give quite the same value, the accuracy of the analysis decreases when large amounts of secondary chlorides are present. As used, the method had an accuracy of approximately ±3%.

Preparation of Pure Monochlorides.—Specially pure samples of the three monochlorides were prepared by the action of redistilled thionyl chloride on the corresponding alcohols, in the presence of pure pyridine (Darzens, *Compt. rend.*, **1911**, **152**, 1314; Clark and Streight, *Trans. Roy. Soc. Canada*, **1929**, **23**, 77; Vogel, *J.*, **1943**, 638). In the synthesis of the corresponding pentane derivatives, this method has been shown to minimise the possibility of rearrangements (Whitmore, Karnatz, and Popkin, *J. Amer. Chem. Soc.*, 1938, **60**, 2540). The secondary alcohols, prepared by the action of aldehydes on the appropriate Grignard reagents, and *n*-hexyl alcohol (B.D.H.) were purified by fractionation at reduced pressure, under nitrogen. The crude chlorides were washed with water and 10% sodium carbonate solution,

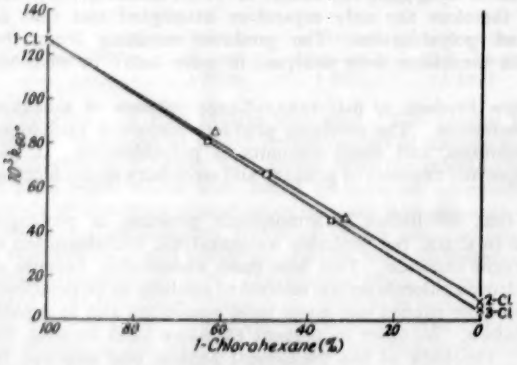

FIG. 1. *Diagram for the analysis of mixtures of the monochlorides from n-hexane.*

× Pure chlorides (1-Cl, 2-Cl, 3-Cl = 1-, 2-, and 3-chlorohexane, respectively).

Synthetic mixtures:
△ 1-Cl + 2-Cl.
□ 1-Cl + 3-Cl.
○ 1-Cl + 2-Cl + 3Cl.

dried ($CaCl_2$), and twice fractionated at reduced pressure. Boiling ranges and refractive indices of the final products, which were completely free from dissolved hydrogen chloride, are shown in Table 3.

TABLE 3. *Characteristics of pure monochlorohexanes.*

	1-Chloro-	2-Chloro-	3-Chloro-
Boiling range	135·5—138°/760 mm.	125—126°/760 mm.	124—125°/760 mm.
	20·0—20·5°/19 mm.	29—30°/24 mm.	23—24°/19 mm.
n_D^{20}	1·4205	1·4162	1·4177

Determination of Rate Constants.—The method devised by Conant and Kirner (*J. Amer. Chem. Soc.*, 1924, **46**, 232) and followed by Hass and Weber (*loc. cit.*) was used, with several important modifications. Thick Pyrex tubes were used as reaction vessels and each was charged with 5 ml. of 0·04M-potassium iodide ("AnalaR," dried at 110°) in anhydrous acetone ("AnalaR," dried over KOH and redistilled), and a thin glass bulb containing a weighed amount (*ca.* 0·001 mole) of the organic chloride. They were sealed off under nitrogen, fitted with thin sheaths of lead foil to exclude light, and placed in the thermostat at 60° (±0·05°) for a preheating period of 1 hr. Reaction was then initiated by breaking the inner bulb against a thick indentation on the bottom of the reaction vessel. After a known time, the residual potassium iodide was determined by titration with 0·003M-potassium iodate, in the presence of hydrochloric acid, the organic halides having first been removed by extraction with chloroform. It was found that a more satisfactory end point was obtained by using only half the volume of concentrated hydrochloric acid suggested by Conant and Kirner (*loc. cit.*).

In preliminary experiments, it was observed that the rate of disappearance of inorganic iodide was greatly increased by the presence of dissolved hydrogen chloride. In such circumstances, the main replacement reaction was accompanied by a side reaction, in which free iodine was produced. Since distillation of the chlorides at atmospheric pressure can result in slight decomposition and contamination of the product with traces of hydrogen chloride, measurements of velocity constants on material so treated are unreliable. Subse-

quently, rigorous precautions, described above, were taken to ensure that all mixtures to be analysed by this method were completely free from hydrogen chloride. With this condition fulfilled, and in the absence of light and oxygen, only the faintest trace of iodine was liberated, even after 48 hours' reaction.

Results.—Conditioning of the surface in thermal chlorinations. When a mixture of hydrocarbon, chlorine, and nitrogen was passed continuously through a "clean" reaction tube, held at a constant high temperature, the proportion of chlorine reacting increased slowly to a steady maximum which was not attained until after 30—60 min. A typical example is shown in Fig. 2. Since oxygen was completely removed from the system before each experiment, this effect must be due to a conditioning of the reaction surface.

After a chlorination there was no appearance of a carbonaceous deposit as reported by Hass, McBee, and Weber (*loc. cit.*) and no other visible change in the condition of the surface of the reaction vessel. However, the reaction surface as produced at *BC* in Fig. 2. was no longer wettable by water or by a mixture of nitric and sulphuric acids at 100°. This indicated that a film had been formed on the surface of the Pyrex glass.

The following properties of this surface film were observed: (i) It could not be removed by prolonged heating in the presence of nitrogen. A reaction vessel in which a chlorination had just been conducted was heated to 300° and kept at this temperature for 5 hr., during which nitrogen was passed over the surface and into a bubbler containing alcoholic silver nitrate solution. The bubbler was changed at hourly intervals, and the contents were examined for

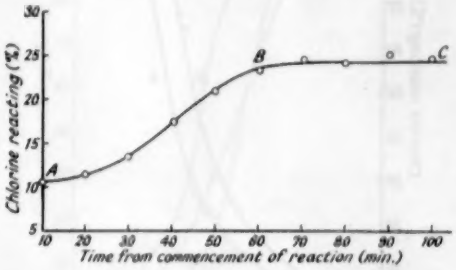

FIG. 2. *Thermal chlorination of* 2:2:4-*trimethylpentane in a clean vessel at* 219°.

silver chloride. During the first hour a faint turbidity appeared in the silver nitrate solution, indicating that chlorine or a compound containing chlorine had been removed from the reaction surface. Thereafter no further evolution of detectable products occurred and at the end of the experiment the surface was still completely unwettable by water. In effect, the reaction vessel had been purged of adsorbed chlorination products but the main surface film had not been removed by this treatment.

(ii) The film could be removed by exposing the heated reaction surface to oxygen. The vessel which had been treated as in (i) was kept at 300° for 3 hr. in a slow stream of oxygen. The exit gas was tested periodically with alcoholic silver nitrate solution and with Schiff's reagent, but neither chlorine compounds nor aldehydes were detected. However, at the end of the experiment the surface was completely wettable by water. Apparently the main film had consisted of a carbon compound which did not contain chlorine, and could be oxidised to volatile products, probably carbon dioxide and water.

(iii) The surface film could also be removed by washing the reaction vessel with concentrated alcoholic potassium hydroxide solution.

After the initial conditioning of the reaction vessel, described above, high- and low-temperature experiments were completely reproducible provided the reaction vessel was not exposed to oxygen or allowed to cool. A typical temperature profile for the thermal chlorination of *n*-hexane is shown in Fig. 3, Curve *A*. The experimental points were obtained in random order, on different occasions and with several different batches of reactants, but the reaction surface, having first been conditioned was kept at temperatures above 190° throughout the series and was not exposed to the atmosphere. When the reaction surface was cleaned, dried, and again conditioned, a further series of experiments with *n*-hexane gave the results shown in Fig. 3, Curve *B*. Though the temperature profile had the same general shape as before, it was displaced by approximately 6°. Since this effect was also observed in two series of experiments with *n*-pentane, it would appear that it is not possible to obtain absolutely

reproducible surface conditions by cleaning and reconditioning. It may be that the treatment with alcoholic potassium hydroxide not only removes the water-repellent film but also affects the physical properties of the Pyrex surface. A change in the total surface area may be involved.

It was found that the best method of ensuring constant surface conditions over a long period was to restrict the cleaning of the reaction vessel at the end of each run to a thorough purging with nitrogen. The coated surface of a conditiond reaction vessel remained completely unchanged throughout the chlorination of a whole series of paraffins provided it was not allowed to cool or exposed to oxygen. Under these conditions, experiments with different hydrocarbons and at different temperatures were fully reproducible in any order.

The sensitivity of these reactions to surface conditions was further demonstrated by the accelerating action of Pyrex glass wool. Typical results for *n*-pentane are shown in Fig. 4. This effect was also observed by Vaughan and Rust (*loc. cit.*) in the chlorination of ethane.

FIG. 3.

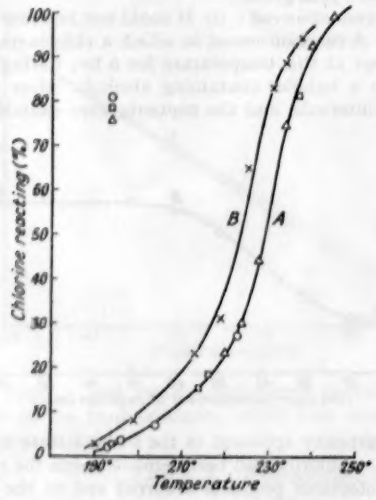

FIG. 4.

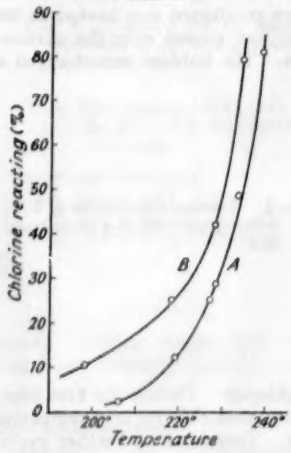

FIG. 3. *Thermal chlorination of* n-*hexane.*
Curve *A*: In a "conditioned" vessel; ○ Series I; □ Series II; △ Series III.
Curve *B*: In same vessel after cleaning and "re-conditioning."

FIG. 4. *Effect of glass wool on the thermal chlorination of* n-*pentane.*
A, Reaction vessel empty. *B*, Reaction vessel packed with glass wool.

Effect of molecular structure on relative rates of thermal chlorination. The C_5—C_8 series of paraffins *n*-pentane, *n*-hexane, *n*-heptane, 2 : 3-dimethylbutane, and 2 : 2 : 4-trimethylpentane were chlorinated under exactly comparable conditions as described in the preceding paragraphs. Results are shown in Figs. 5 and 6 in the form of temperature profiles.

It seemed most likely that the observed differences in reactivity were due only to differences in the molecular structure of the paraffins, but various other possibilities were considered and eliminated. (i) Repeated cross-checking of results showed that surface conditions remained constant throughout the whole series of experiments. (ii) In separate experiments, the organic products resulting from the chlorination of each of the paraffins were collected and examined by fractional distillation. In every case, di- and poly-chlorides constituted less than 5% of the total volume of alkyl chlorides. Therefore the observed differences in reactivity could not have been due to initial chlorination products, from the various paraffins, undergoing further chlorination at different rates. (iii) It was also important to verify that substitution was the chief reaction taking place, since preferential decompositon of certain monochlorides to olefins and hydrogen chloride would have affected the comparisons. A careful examination of the analytical results showed that, over the whole range of temperature investigated, the ratio moles of hydrogen chloride produced/moles of chlorine consumed was

approximately unity, for each of the paraffins. Typical results, for reactions in the neighbourhood of 230°, are shown in Table 4.

TABLE 4. *Equivalence of chlorine consumed and hydrogen chloride produced* (units: millimoles/min.).

Paraffin	Temp.	Cl_2 entering vessel	Cl_2 recovered unchanged	Cl_2 consumed	HCl produced	HCl produced / Cl_2 consumed
n-Pentane	226°	0·985	0·747	0·238	0·237	0·995
n-Hexane	231	0·985	0·171	0·814	0·803	0·986
n-Heptane	232	0·985	0·127	0·858	0·863	1·006
2 : 3-Dimethylbutane ...	228	0·985	0·697	0·288	0·296	1·026
2 : 2 : 4-Trimethylpentane	230	0·985	0·520	0·465	0·471	1·013

Since substitution followed by pyrolysis produces two molecules of hydrogen chloride per molecule of chlorine consumed, the close approximation of the ratio to unity indicates that pyrolysis did not occur to any appreciable extent. In the case of 2 : 3-dimethylbutane, the

FIG. 5.

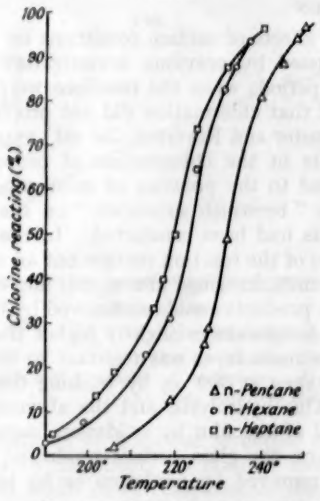

FIG. 6.

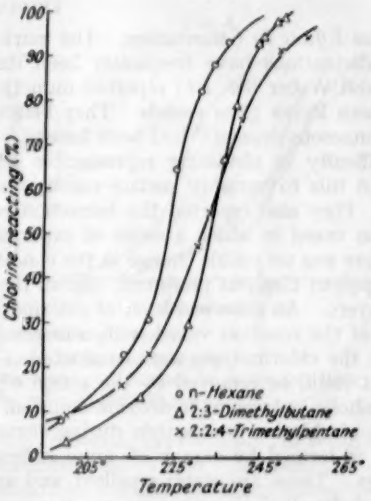

FIG. 5. *Effect of chain-lengthening on relative rates of thermal chlorination.*

FIG. 6. *Effect of chain-branching on relative rates of thermal chlorination.*

differences between hydrogen chloride produced and chlorine consumed were just outside the limits of experimental error (±2%), over the whole temperature range, indicating that slight decomposition of the monochlorides of this particular hydrocarbon did occur. However, the amounts of "excess HCl" found were so small that this factor could not materially affect the comparisons. Consequently, the temperature profile was not corrected.

The general conclusion is that the results shown in Figs. 5 and 6 indicate a marked variation in reactivity depending only on the molecular structure of the paraffins.

Photochemical chlorination of n-*hexane.* With the same rates of flow as in the thermal experiments, high percentage conversions of chlorine were obtained by illumination of the reaction tube with white light, at reaction temperatures as low as 80°, which was a lower limit set by vapour-pressure considerations. A typical temperature profile is shown in Fig. 7. Like the thermal reactions, the photochemical process was extremely susceptible to inhibition by oxygen and to surface conditions. The slow build-up to maximum rate in a clean reaction vessel, and the formation of water-repellent surface films were again observed. There was no evidence for decomposition of initial chlorination products, and, as in the thermal reactions, di- and poly-substituted compounds constituted less than 5% of the total volume of alkyl chlorides.

Examination of the chlorination products of n-*hexane.* The object was to determine the

relative amounts of primary and secondary monochlorides produced in reactions at two widely different temperatures, under conditions which otherwise were strictly comparable. Large volumes of the hydrocarbon were chlorinated photochemically at 88°, and thermally at 238°. In both sets of conditions, 94% of the chlorine in the gaseous mixture was being consumed (see Figs. 5 and 7) and monosubstitution was the only important reaction. The mixtures of monochlorides were analysed by the method previously described and the analyses confirmed by fractional distillation. The results are shown Table 5. Since Hass, McBee, and Weber (*loc. cit.*) have shown that the isomeric ratios are unaffected by illumination, the increase of primary halide in the reaction products is apparently due only to the rise in reaction temperature.

TABLE 5. *Analyses of the monochlorination products of* n-*hexane.*

	Kinetic analysis		Distillation analysis	
Reaction temp.	Primary, %	Secondary, %	Primary, %	Secondary, %
88°	19·8 (± 3·0)	80·2 (±3·0)	25 (±5)	75 (±5)
238	24·6 (± 3·0)	75·4 (±3·0)	31 (±5)	69 (±5)

DISCUSSION

Surface Effects in Chlorination.—The marked effects of surface conditions on vapour-phase chlorinations have frequently been discussed by previous investigators. Hass, McBee, and Weber (*loc. cit.*) reported induction periods when the reactions were carried out in clean Pyrex glass vessels. They believed that chlorination did not proceed until a " carbonaceous deposit " had been formed. Yuster and Reyerson (*loc. cit.*) experienced great difficulty in obtaining reproducible results in the chlorination of propane and attributed this to variably surface conditions and to the presence of small amounts of oxygen. They also reported the formation of a " brownish substance " on the wall of a reaction vessel in which a series of experiments had been conducted. In the present work, there was no visible change in the condition of the reaction surface but an invisible, water-repellent film was produced. From the results described above, this film consisted of two layers. An adsorbed layer of chlorination products could be removed by thorough purging of the reaction vessel with nitrogen at temperatures slightly higher than those at which the chlorinations were conducted. The main layer was resistant to this treatment but could be removed by the action of oxygen at 300° or by washing the surface with alcoholic potassium hydroxide solution. This hydrolysis, and the absence of any evidence of chlorine compounds during removal of the film by oxidation, suggest that the film is formed by attack of alkyl radicals on the glass surface producing Si–O–R groupings. These are water-repellent and are removed by oxidation or by hydrolysis with alcoholic alkali.

The accelerating action of glass wool also observed by Vaughan and Rust (*loc. cit.*) in the chlorination of ethane indicates that, for the thermal chlorination, chains are initiated on the surface. Pease and Walz (*loc. cit.*) and Yuster and Reyerson (*loc. cit.*) showed that the observed reaction rate could not be explained on the basis of initiation by homogeneous thermal dissociation of chlorine molecules. The change in reaction surface, observed in the present work, suggests a two-fold influence on the rate of chlorination: (i) until the surface has been completely coated with alkyl groups, the rate of reaction is decreased by the removal of chain-carriers in the side-reaction with the glass; (ii) the surface film may be more effective than clean Pyrex glass in initiating chains in the thermal chlorination.

Yuster and Reyerson (*loc. cit.*) reported a progressive decrease in the rate of chlorination when long reaction times were employed, and attributed this to fouling of the surface by highly chlorinated products. In the present dynamic experiments the rate showed no tendency to decrease with time.

Effects of Molecular Structure on Monochlorination Rates.—The main result of the present investigation is that the reaction of chlorine atoms with paraffin hydrocarbons is sensitive to molecular structure. Comparison between *n*-pentane, *n*-hexane, and *n*-heptane indicates clearly that, in this range, the ease of chlorination increases with chain length. The temperature profiles obtained by Vaughan and Rust (*loc. cit.*) for

ethane and propane, and by Topchiev, Krentsel, and Andreev (*Doklady Akad. Nauk S.S.S.R.*, 1952, **85**, 823; *Chem. Abs.*, 1952, **46**, 10,836) indicate that the lower members of the homologous series may be even less reactive than *n*-pentane. This point is illustrated in Fig. 8, but it must be emphasised that strict comparisons between the present and previous work are not possible, since allowance cannot be made for differences in important factors such as surface conditions, size of reaction vessel, contact time, and composition of the gaseous mixtures. However, it does appear that, over the range of *n*-paraffins C_2—C_7 there is a general increase in reactivity towards chlorine as the chain lengthens. A similar effect has been observed by Groll and Hearne (*Ind. Eng. Chem.*, 1939, **31**, 1530) in the chlorination of the series of olefins ethylene, propylene, but-2-ene, and pent-2-ene.

The results shown in Fig. 6 indicate that reactivity is decreased by chain-branching. Under the conditions studied, 2 : 3-dimethylbutane is appreciably less reactive than *n*-hexane. Although *n*-octane has not been studied, it is obvious from the general trend of the results that it would be at least as reactive as *n*-heptane. Yet *iso*octane (2 : 2 : 4-trimethylpentane), over the major part of the temperature range investigated, is appreciably less reactive than *n*-hexane.

FIG. 7.

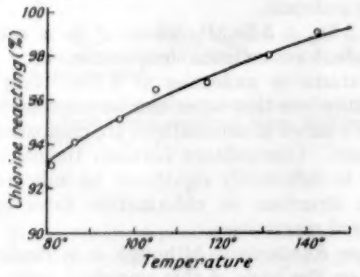

FIG. 8.

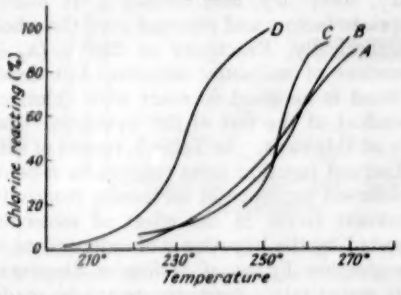

FIG. 7. *Photochemical chlorination of* n-*hexane.*

FIG. 8. *Thermal chlorination of the lower paraffins.*
A, Ethane. *B*, Propane. *C*, *n*-Butane. *D*, *n*-Pentane. (*A*, *B*, from Vaughan and Rust, *loc. cit.* *C*, from Topchiev *et al.*, *loc. cit.* *D*, present work.)

These effects of molecular structure on monochlorination rates are, in some respects, analogous to the effects on rates of slow oxidation below 300°. Although it is again difficult to make strict comparisons, the indications are that in chlorination the effects are not nearly so pronounced as in oxidation. On the basis of the criterion used by Cullis and Hinshelwood (*Discuss. Faraday Soc.*, 1947, **2**, 117) and by Mulcahy (*ibid.*, p. 128), the rate of oxidation, on average, increases by a factor of about 5 for each successive member of the homologous series.

As is shown in Table 6, there is no evidence for differences of this magnitude in vapour-phase chlorination.

TABLE 6.

	Cl_2 reacting, %, at :					Cl_2 reacting, %, at :					Cl_2 reacting, %, at :			
Paraffin	210°	220°	230°	240°	Paraffin	210°	220°	230°	240°	Paraffin	210°	220°	230°	240°
n-Pentane	5	13	37	81	*n*-Hexane	16	40	81	96	*n*-Heptane	23	50	85	96

The same conclusion is reached when the positions of the temperature profiles, for the different paraffins, are compared with minimum temperatures of perceptible combustion, as determined by Callendar (*Engineering*, 1927, **123**, 147).

Differences between chlorination and oxidation are even more pronounced when the effect of molecular branching is considered. For example, Cullis and Hinshelwood (*loc. cit.*) found that the rate of oxidation of *n*-hexane was approximately 1600 times that of 2 : 3-dimethylbutane. Even allowing for the fact that the two systems are far from being strictly comparable, the difference in reactivity between these isomers, observed in the present work, is at the most a factor of 5. Pope, Dykstra, and Edgar (*J. Amer. Chem.*

Soc., 1929, **51**, 1875, 2203) moreover found that the oxidation of 2 : 2 : 4-trimethylpentane required a temperature of 500°, compared with 200—250° for straight-chain paraffins of comparable molecular weight. Yet the chlorination of this compound occurs in the same temperature range as for the other hydrocarbons investigated.

Hypothesis of Independent Reactivity of Different C–H *Bonds.*—At present, the kinetics are too complex to warrant discussion in terms of the highly formalised treatment applicable for simple molecules. Useful discussion of the relations between the reactivities of the different molecules can be made in terms of the simple hypothesis of independent reactivities of the C–H bonds, and of departures from such independent reactivities. Hass, McBee, and Weber (*loc. cit.*) have shown that the rates of substitution at primary, secondary, and tertiary C–H bonds increase in that order. With increasing temperature, the relative rates approach a ratio of 1 : 1 : 1. For purposes of computation the relative reactivities of primary, secondary, and tertiary hydrogen atoms at different temperatures can be taken from figures they supply. At 230° in the vapour phase these are approximately 1 : 3·5 : 5·2. These ratios are not completely independent of the total molecular structure, but in testing the hypothesis this refinement can be temporarily neglected. On the hypothesis of independent reactivities, the respective numbers n_1, n_2, n_3 of primary, secondary, and tertiary C–H bonds in each molecule are multiplied by the appropriate factors and summed over the whole molecule.

Algebraically, Reactivity at 230° $= (n_1 + 3{\cdot}5n_2 + 5{\cdot}2n_3)P$, where P is a constant independent of molecular structure but dependent on collision frequencies, etc. Each C–H bond is assumed to react with chlorine atoms or molecules at a rate completely independent of the rest of the structure. *Relative* reaction rates can be expressed very simply on this basis. In Table 7, results of such a series of summations are compared with the observed reaction rates relative to *n*-pentane. Concordance between the calculated and observed sequence of increasing reactivity is sufficiently significant to indicate that a dominant factor in the effect of molecular structure on chlorination rates can be interpreted by the hypothesis of independent bond reactivities.

Co-operative Effects of Molecular Structure on Reactivity.—Although it is doubtful if strictly quantitative comparisons can be made on the basis of this empirical summation, it is noteworthy that *n*-hexane and *n*-heptane appear to be more reactive than would be predicted from the simple additivity rule. This discrepancy would be even more evident if allowance had been made in the calculations for the dependence of the rate factors of secondary hydrogen atoms on overall molecular structure. Thus, even in monochlorination, for which the reaction steps seem fairly simple, lengthening the carbon skeleton appears to increase the overall reaction rate above the additive value. Possibly this may be due to vibration-coupling in the unbranched portions of the molecules (Ubbelohde, *Proc. Roy. Soc.*, 1935, *A*, **152**, 354; *Rev. l'Inst. franç. Pétrole*, 1949, **4**, 488). Nevertheless, compared with oxidation of the same hydrocarbons, the overall chlorination rates are much less sensitive to molecular structure.

TABLE 7. *Comparison of calculated and observed rates of thermal chlorination at* 230°. (*Hypothesis of independent bond reactivity.*)

Paraffin skeleton	Calculated: Relative rates of substitution of H atoms n_1	$3{\cdot}5n_2$	$5{\cdot}2n_3$	Total	Calculated: Reaction rate, relative to *n*-pentane	Observed: Chlorine reacted at 230°, %	Observed: Reaction rate, relative to *n*-pentane
C–C–C–C–C	6	21	—	27	(1·00)	37	(1·00)
C–C–C–C–C–C ...	6	28	—	34	1·26	81	2·19
C–C–C–C–C–C–C ...	6	35	—	41	1·52	85	2·30
C–C(C)–C–C	12	—	10·4	22·4	0·83	37	1·00
C–C(C)(C)–C–C	15	7	5·2	27·2	1·00	47	1·27

Effect of Chain Length and of Temperature on the Relative Reactivities of Primary and Secondary C–H *Groups.*—As stated above, the relative reactivities of primary and

secondary C–H groups are not strictly independent of the overall structure, or of the temperature. On the additive hypothesis, in *n*-hexane, the relative reactivity should be

$$\frac{\text{Secondary}}{\text{Primary}} = \frac{\text{Yield of secondary chlorides} \times 6}{\text{Yield of primary chlorides} \times 8}$$

Substitution of the results obtained by the kinetic method of analysis gives 2·30 at 238° and 3·03 at 88°. Both these figures are smaller than the value 3·5 taken for purposes of illustration in Table 7 and they show a trend towards unity as the temperature rises. Similar trends can be derived from the large body of figures given by Hass, McBee, and Weber, but some care is needed in the selection. In the present work, the large excess of hydrocarbon and of diluent nitrogen, and the short contact time, ensured that only a small amount of monochloride underwent further chlorination. Therefore the results are not complicated by preferential removal of certain initial products of chlorination by further reaction.

In Fig. 9 the results now obtained have been compared with those obtained by Hass and his co-workers (*loc. cit.*) for other paraffins, selected for conditions where less than

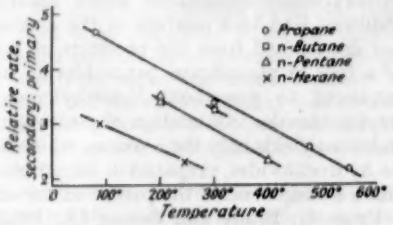

FIG. 9. *Effect of chain-lengthening on relative rates of substitution of primary and secondary hydrogen atoms.*

(Values for hexane, present work; others selected from results of Hass, McBee, and Weber, *loc. cit.*)

9% of the reaction products consisted of polychlorides. It is evident that the reactivity of secondary relative to primary hydrogen appears to decrease as the chain lengthens, when comparisons are made at the same temperature. The trend is towards unity as the temperature rises, for all the examples given. This trend with chain length is in excellent agreement with the results obtained by McBee, Hass, and Pianfetti (*Ind. Eng. Chem.*, 1941, **33**, 185) in the chlorination of the series propane, *n*-pentane, and *n*-heptane at a pressure of 1000 lb. per sq. in. These workers tentatively attributed the trend either to slight differences in activation energies, due presumably to variation in bond energies along the chain, or to steric factors. Our knowledge of bond energies is still far from complete and hence the former possibility cannot be further discussed. However, recent physical measurements (McCoubrey, McCrea, and Ubbelohde, *J.*, 1951, 1961; Cummings, McCoubrey, and Ubbelohde, *J.*, 1952, 2725; Cummings and Ubbelohde, *J.*, 1953, 3751) have shown that the normal paraffins, in the range C_5—C_8, are substantially crumpled in the vapour phase. Consequently, it seems likely that the trend of relative reactivities with chain length observed is due to steric factors. In partially crumpled configurations, some of the secondary C–H bonds may be protected by other parts of the molecule from attack by chlorine atoms. This could lead to the observed decrease in relative reactivity of secondary C–H, and the effect would be expected to become more pronounced as the chain lengthened.

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The Beckmann Rearrangement of Substituted Benzylideneacetone Oximes.

By R. E. Corbett and C. L. Davey.

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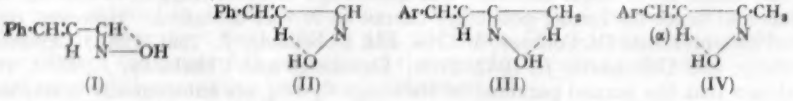
The synthesis and Beckmann rearrangement of a number of *para*-substituted benzylideneacetone oximes have been studied. *N*-*p*-Methoxy- and *N*-*p*-nitro-styrylacetamide have been prepared.

N-Styrylacetamide has been prepared by the Beckmann rearrangement of benzylideneacetone α-oxime (Auwers *et al.*, *J. pr. Chem.*, 1932, **133**, 154) and this method has now been applied to the synthesis of *N*-*p*-methoxy- and *N*-*p*-nitro-styrylacetamide.

Oximation of benzylideneacetone under both acidic and alkaline conditions yields only the α-oxime. The β-oxime has been obtained by neutralisation of a hydrochloride prepared from the α-oxime in absolute ethanol (Auwers *et al.*, *loc. cit.*). Oximation of *p*-methoxybenzylideneacetone under alkaline conditions gives the α-oxime, but acidic conditions lead to a mixture of the α- and the β-oxime (65 : 35). These structures have been determined from the products of Beckmann rearrangement of the oximes. Under the action of phosphorus pentachloride, the β-oxime of *p*-methoxybenzylideneacetone is rearranged to *p*-methoxy-*N*-methylcinnamamide, and the α-oxime to *N*-*p*-methoxystyrylacetamide. Oximation of *p*-nitrobenzylideneacetone under both acidic and alkaline conditions yields only the α-oxime, which has been isomerized to *N*-*p*-nitrostyrylacetamide. The hydrochlorides, prepared in anhydrous ether, and the benzoates of the aforementioned oximes all regenerated the parent oxime on mild alkaline hydrolysis.

Recently, Brady and Benger (*J.*, 1953, **3612**) have suggested that hydrogen bonding plays an important part in stabilizing one isomeride relative to the other in a series of substituted cinnamaldoximes; *e.g.*, cinnamaldehyde on oximation in alkaline solution gives a mixture of the α- and the β-oxime in which the latter predominates, but *o*-, *m*-, and *p*-nitrocinnamaldehydes under these conditions give mainly the α-aldoximes. Structures (I) and (II) are proposed for the possible isomerides. A similar explanation can account for our observations concerning the stability of the benzylideneacetone oximes already described. In these cases it is suggested that a lone pair of electrons of the oxygen atom may be associated either with the methine-hydrogen H_a (IV) or with a hydrogen of the terminal methyl group (III).



(I) (II) (III) (IV)

The α-isomeride (III) represents the stable form of benzylideneacetone oxime, and the only form of *p*-nitrobenzylideneacetone oxime. In the latter case the electron-withdrawing influence of the nitro-group will militate against hydrogen bonding, although a hydrogen bond with the most electron-deficient hydrogen atom should be possible. Because of the inductive and possible hyperconjugative effects of the terminal methyl group, hydrogen bonding may take place with a methyl hydrogen (III). This could provide an explanation for the occurrence of only the α-isomeride of *p*-nitrobenzylideneacetone oxime. With an electron-repelling methoxyl group in the *para*-position, which should help to promote hydrogen bonding, *p*-methoxybenzylideneacetone gives a mixture of isomerides, with the α-form still predominating.

Experimental

p-*Methoxybenzylideneacetone α-Oxime.*—Hydroxylamine hydrochloride (2 g.) and *p*-methoxybenzylideneacetone (1 g.) (*Org. Synth.*, Coll. Vol. I, 2nd Edn., p. 77) were added to aqueous sodium hydroxide (20 c.c.; 5%), and sufficient alcohol (10 c.c.) to give a clear solution was added. After

being heated on a water-bath for 15 min. the mixture was diluted with water (200 c.c.), and the oxime separated. Recrystallisation from xylene gave colourless needles of the α-oxime, m. p. 123—124°. Harries and Tietz (*Annalen*, 1902, **320**, 242) record m. p. 119—120° for this compound: their specimen obviously contained some of the β-isomeride. p-*Methoxybenzylideneacetone α-oxime benzoate* (prepared by use of benzoyl chloride in pyridine) crystallised from methanol in plates, m. p. 125° (Found: C, 73·1; H, 5·8. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8%).

p-*Methoxybenzylideneacetone β-Oxime.*—*p*-Methoxybenzylideneacetone (5 g.) and hydroxylamine hydrochloride (5 g.) in absolute alcohol (50 c.c.) were refluxed for 5 hr. and then kept overnight in an ice-chest, a yellow precipitate of the oxime hydrochloride separating. Hydrolysis of this with water (50 c.c.) liberated p-*methoxybenzylideneacetone β-oxime* (35% yield) which after recrystallisation from ethanol had m. p. 157—158° (Found: C, 68·8; H, 6·9; N, 6·9. $C_{11}H_{13}O_2N$ requires C, 68·75; H, 6·8; N, 7·3%). The filtrate after removal of the above hydrochloride was poured into water (150 c.c.), and the resulting precipitate of the α-oxime collected. It had m. p. 123—124° after recrystallisation from xylene (yield 65%). p-*Methoxybenzylideneacetone β-oxime benzoate*, prepared by the method described for the α-oxime, crystallised as plates from methanol, m. p. 125°, depressed on admixture with the benzoate from the α-oxime (Found: C, 73·0; H, 5·8; N, 4·6. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·75%).

N-p-*Methoxystyrylacetamide.*—*p*-Methoxybenzylideneacetone α-oxime (2 g.) was dissolved in dry ether, phosphorus pentachloride (2 g.) added, and the mixture shaken for 20 min., separation of a dull red powder from the ether layer then being complete. Ether (20 c.c.) and chipped ice (20 g.) were added, and the shaking continued until the decomposition of the complex was complete. The ether layer was separated, washed with water, and dried (Na_2SO_4). The ether solution was concentrated until a red oil separated, and the ethereal liquors were decanted therefrom. Complete removal of the ether gave oily crystals of N-p-*methoxystyrylacetamide*, which crystallised as small plates, m. p. 114—115°, after repeated crystallisation from benzene (Found: C, 68·9; H, 6·5. $C_{11}H_{13}O_2N$ requires C, 68·75; H, 6·8%).

Rearrangement of *p*-methoxybenzylideneacetone β-oxime in the same manner gave p-*methoxy*-N-*methylcinnamamide*, m. p. 164° (from water), undepressed with a specimen prepared from *p*-methoxycinnamoyl chloride and methylamine (Found: C, 68·9; H, 6·8. $C_{11}H_{13}O_2N$ requires C, 68·75; H, 6·8%).

p-*Nitrobenzylideneacetone.*—*p*-Nitrobenzaldehyde (1 g.) was dissolved in acetone (12 c.c.), and the solution cooled below 5°. An aqueous solution of sodium hydroxide (1·2 c.c.; 1%) was added dropwise with stirring, which was continued for a further 15 min., and the solution was then made acid with 2N-sulphuric acid. After removal of most of the acetone by distillation, the solution of 4-hydroxy-4-*p*-nitrophenylbutan-2-one was heated with N-sulphuric acid (7 c.c.). *p*-Nitrobenzylideneacetone separated and after crystallisation from alcohol had m. p. 110° (Baeyer and Becker, *Ber.*, 1883, **16**, 1968, record m. p. 110°). Oximation by the methods already described gave in each case p-*nitrobenzylideneacetone α-oxime*, m. p. 185° after crystallisation from ethanol (Found: C, 58·85; H, 4·85; N, 13·45. $C_{10}H_{10}O_3N_2$ requires C, 58·25; H, 4·85; N, 13·6%); its *benzoate*, prepared by use of benzoyl chloride in pyridine, crystallised from ethanol in lemon-yellow needles, m. p. 155° (Found: C, 65·9; H, 4·1. $C_{17}H_{14}O_4N_2$ requires C, 65·8; H, 4·5%).

N-p-*Nitrostyrylacetamide.*—*p*-Nitrobenzylideneacetone α-oxime (5 g.) was dissolved in dry ether (100 c.c.), phosphorus pentachloride (5 g.) added, and the mixture shaken for 2 hr., then poured on crushed ice (20 g.); the ether layer was separated, washed with water, and dried (Na_2SO_4). Evaporation gave N-p-*nitrostyrylacetamide* as a bright orange microcrystalline solid, m. p. 155°, after crystallisation from benzene (Found: C, 58·5; H, 4·4; N, 13·3. $C_{10}H_{10}O_3N_2$ requires C, 58·25; H, 4·85; N, 13·6%). N-*Methyl*-p-*nitrocinnamamide*, synthesised by reaction of *p*-nitrocinnamoyl chloride with methylamine, had m. p. 203—204° (from ethanol) (Found: C, 57·75; H, 5·1; N, 13·4. $C_{10}H_{10}O_3N_2$ requires C, 58·25; H, 4·85; N, 13·6%).

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The Behaviour of Acetic Anhydride and Benzoic Anhydride in Sulphuric Acid.

By J. A. Leisten.

[Reprint Order No. 5695.]

Acetic and benzoic anhydride have been shown to extract water from sulphuric acid, and from dilute oleum, to form the corresponding acidium ions, $Me{\cdot}CO_2H_2^+$ and $Ph{\cdot}CO_2H_2^+$. The bearing of this result on the mechanism of the hydrolysis of esters by sulphuric acid is discussed.

The solutes acetic anhydride and benzoic anhydride in sulphuric acid of maximal freezing point were found by Gillespie (*J.*, 1950, 2997) to give approximately four-fold depressions of the freezing point. The suggested explanation of these results is given by equation (1) (R = Me or Ph throughout this paper). An alternative explanation summarised by equation (2), was rejected on the grounds that it required an improbable mechanism.

$$(R{\cdot}CO)_2O + 2H_2SO_4 = R{\cdot}CO^+ + R{\cdot}CO_2H_2^+ + 2HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$
$$(R{\cdot}CO)_2O + 3H_2SO_4 = 2R{\cdot}CO{\cdot}HSO_4 + H_3O^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

It was subsequently shown that the electrical conductivities of solutions of these anhydrides in sulphuric acid correspond more closely to the formation of one than of two hydrogen sulphate ions per molecule of anhydride, supporting equation (2) rather than (1); it was concluded that the mode of ionisation of the anhydrides had not been established (Gillespie and Wasif, unpublished experiments; Gillespie and Leisten, *Quart. Reviews*, 1954, **8**, 40).

It has recently been found that phthalic anhydride produces a less-than-unit depression of the freezing point of aqueous sulphuric acid, indicating that this anhydride extracts water from the solvent (Brayford and Wyatt, personal communication). It thus becomes necessary to consider a third explanation of the four-fold freezing-point depression of acetic acid and benzoic anhydride in 100% sulphuric acid :

$$(R{\cdot}CO)_2O + 3H_2SO_4 = 2R{\cdot}CO_2H_2^+ + HS_2O_7^- + HSO_4^- \quad . \quad . \quad . \quad . \quad (3)$$

Ionisation according to equation (3) produces only one hydrogen sulphate ion per molecule of anhydride and is thus consistent with the conductivity data. Equation (3) may be considered as the sum of (4) and (5)

$$(R{\cdot}CO)_2O + 3H_2SO_4 = 2R{\cdot}CO_2H_2^+ + 2HSO_4^- + SO_3 \quad . \quad . \quad . \quad . \quad . \quad (4)$$
$$SO_3 + HSO_4^- = HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Expression (4) represents the extraction of water from the solvent by the anhydride, and the addition of protons to the carboxylic acid formed. Equation (5) follows from the work of Brand (*J.*, 1946, 880) and of Gillespie (*J.*, 1950, 2516), who showed that hydrogen sulphate ions are largely converted into hydrogen disulphate ions in dilute oleum.

The present work shows that both anhydrides react with 100% sulphuric acid according to equation (3); and that although the overall equation differs if the solvent is aqueous sulphuric acid, or if the solvent is dilute oleum, yet in all cases the behaviour is essentially the same : water is extracted from the solvent, and carboxylic acidium ions are formed.

Experimental

Materials.—" AnalaR " acetic anhydride was fractionally distilled and the fraction of b. p. 139·0—139·5° was collected. Benzoic anhydride was precipitated three times from benzene solution by the addition of light petroleum : it had m. p. 42—43°. The acetic acid used was a fresh " AnalaR " sample, and the benzoic acid had m. p. 121·5—122°. " AnalaR " ammonium sulphate was dried at 130° for 2 hr. The materials were stored over phosphoric anhydride.

Freezing-point Measurements.—The cryoscopic technique and the method of computing results were similar to those used by Gillespie and Leisten (*J.*, 1954, 1).

Results

TABLE 1. *Freezing-point measurements in aqueous sulphuric acid.*

Acetic anhydride				Benzoic anhydride			
Δm	F. p.	$\Delta\theta$	*i*-Factor	Δm	F. p.	$\Delta\theta$	*i*-Factor
—	8·640°	—	—	—	8·758°	—	—
0·0672	7·800	0·840°	2·08	0·01224	8·605	0·153°	2·08

TABLE 2. *The addition of water to anhydride solutions in 100% sulphuric acid.*

Acetic anhydride (0·161*m*)				Benzoic anhydride (0·0423*m*)			
Molality of H_2O (Δm)	Increment of Δm	F. p.	*i*-Factor *	Molality of H_2O (Δm)	Increment of Δm	F. p.	*i*-Factor
—	—	6·815°	—	—	—	9·559°	—
0·160	0·160	6·716	0·10	0·0359	0·0359	9·594	−0·16
0·210	0·050	6·264	1·51 †	0·0522	0·0163	9·512	—
—	—	—	—	0·0815	0·0293	9·223	1·64 †

* The *i*-factors are computed for *increments* of molality and freezing-point depression.
† The solute water produces a depression which is slightly less than two-fold in pure sulphuric acid, and considerably less than two-fold in solutions containing a high concentration of hydrogen sulphate ion (Gillespie, *J.*, 1950, 2493).

TABLE 3. *Freezing point of solutions of acetic anhydride and of benzoic anhydride in oleum.*

Acetic anhydride		Benzoic anhydride	
Initial molality of $H_2S_2O_7$ = 0·1363		Initial molality of $H_2S_2O_7$ = 0·1328	
Molality of $(Me{\cdot}CO)_2O$	F. p.	Molality of $(Ph{\cdot}CO)_2O$	F. p.
—	9·460°	—	9·487°
0·0131	9·301	0·0092	9·373
0·0423	8·867	0·0228	9·183
0·0600	8·557	0·0424	8·860
0·0793	8·214	0·0598	8·549

TABLE 4. *Freezing point of oleum solutions containing acetic acid.*

$Me{\cdot}CO_2H$ (*m*)	$H_2S_2O_7$ (*m*)	F. p.	$Me{\cdot}CO_2H$ (*m*)	$H_2S_2O_7$ (*m*)	F. p.	$Me{\cdot}CO_2H$ (*m*)	$H_2S_2O_7$ (*m*)	F. p.
—	0·1420	9·420°	—	0·1822	9·136°	—	0·2273	8·812°
0·0262	0·1158	9·353	0·0348	0·1474	9·065	0·0527	0·1746	8·688
0·0592	0·0828	9·233	0·0663	0·1159	8·956	0·0926	0·1347	8·535
0·1147	0·0273	8·915	0·1067	0·0755	8·761	0·1246	0·1027	8·385
—	—	—	0·1596	0·0226	8·420	0·1557	0·0716	8·211

TABLE 5. *Freezing point of oleum solutions containing benzoic acid.*

$Ph{\cdot}CO_2H$ (*m*)	$H_2S_2O_7$ (*m*)	F. p.	$Ph{\cdot}CO_2H$ (*m*)	$H_2S_2O_7$ (*m*)	F. p.	$Ph{\cdot}CO_2H$ (*m*)	$H_2S_2O_7$ (*m*)	F. p.
—	0·1012	9·708°	—	0·1611	9·288°	—	0·2047	8·975°
0·0163	0·0849	9·663	0·0217	0·1394	9·232	0·0113	0·1934	8·945
0·0321	0·0691	9·599	0·0566	0·1045	9·095	0·0340	0·1707	8·885
0·0545	0·0467	9·483	0·0863	0·0748	8·945	0·0607	0·1440	8·786
0·0912	0·0100	9·235	0·1133	0·0478	8·772	0·0975	0·1072	8·604
—	—	—	—	—	—	0·1523	0·0524	8·269

TABLE 6. *Freezing point of oleum solutions containing ammonium sulphate.*

Molality of $NH_4HS_2O_7$	—	0·0371	0·0791	0·1143
Molality of $H_2S_2O_7$ *	0·1152	0·0781	0·0361	0·0009
F. p.	9·610°	9·513	9·317	9·079

* Uncorrected for sulphuric acid formed as in eqn. (13).

It is shown in Table 1 that, in slightly aqueous (99·8%) sulphuric acid, acetic and benzoic anhydrides give two-fold depressions of the f. p. No anhydride could be isolated or detected when the solutions were diluted with water. These results appear to have only one reasonable interpretation: that in aqueous sulphuric acid, the anhydrides are hydrolysed as follows.

$$(R{\cdot}CO)_2O + H_2SO_4 + H_3O^+ = 2R{\cdot}CO_2H_2^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The cryoscopic results are consistent with expression (6), because although three particles are produced per molecule of anhydride, a hydroxonium ion is at the same time removed from the aqueous solvent.

Table 2 shows the effect of adding water to solutions of the anhydrides in 100% sulphuric acid. The addition of an amount of water equimolecular to that of the anhydride has no significant effect on the f. p. of the solution; subsequent additions produce freezing-point depressions that are normal for the solute water. These results are consistent with equations (1) and (3) but not with equation (2). For supposing that the ionisation in 100% sulphuric acid is according to (1), or (2), or (3), the reaction with an equimolecular amount of water must, in view of the experiments in aqueous sulphuric acid, be represented by equations (7), or (8), or (9), respectively.

$$R{\cdot}CO^{+} + H_2O = R{\cdot}CO_2H_2^{+} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$R{\cdot}CO{\cdot}HSO_4 + H_2O = R{\cdot}CO_2H_2^{+} + HSO_4^{-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$HS_2O_7^{-} + H_2O = H_2SO_4 + HSO_4^{-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

The reactions (7) and (9) cause no change in the total number of solute particles. But (8) would lead to a unit depression of the f. p.; moreover, by comparing equations (2) and (8) it is

FIG. 1. *Freezing point of solutions of acetic anhydride in oleum.*

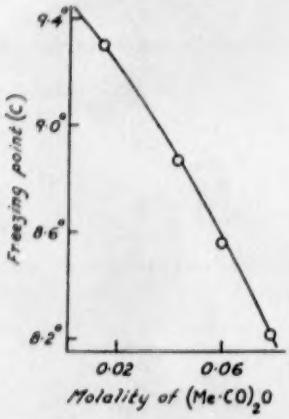
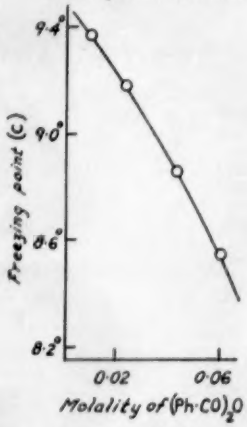


FIG. 2. *Freezing point of solutions of benzoic anhydride in oleum.*



seen that the addition of a further equimolar quantity of water should also produce a unit depression of the f. p. Equation (2) is therefore excluded as an explanation of the cryoscopic behaviour of the anhydrides in 100% sulphuric acid: the remaining results distinguish between (1) and (3).

In Fig. 1, the curve shows the changes of f. p. that would occur if amounts of acetic acid were added to, and half the molar amounts of water were subtracted from, an oleum solvent. Such additions and subtractions are stoicheiometrically equivalent to additions of acetic anhydride. The experimental points in Fig. 1 relate to actual additions of acetic anhydride (Table 3). Similar results are shown for benzoic anhydride in Fig. 2.

The derivation of the curve in Fig. 1 will be illustrated by calculating one point on it. Suppose that the oleum solvent, in which the molality of disulphuric acid is 0·1363, is made 0·1000*m* with respect to acetic acid. On subtracting a 0·0500 molal quantity of water from this solution, the molality of disulphuric acid will become approximately 0·1863, in accordance with the equation: $2H_2SO_4 - H_2O = H_2S_2O_7$. This molality is approximate because the removal of water from the solvent to form disulphuric acid decreases the amount of sulphuric acid in the solution. The exact molality of disulphuric acid will be 0·1881, and that of the acetic acid 0·1010. The f. p. of this solution may be found by interpolation, using the results in Table 4 on the f. p.s of acetic acid solutions in oleum and Gillespie's data on the f. p.s of solutions of disulphuric acid in sulphuric acid (*loc. cit.*). The required f. p. is 8·754°: this is plotted against 0·0500 on the abscissa.

The coincidence of the experimental points and the curve shows that acetic acid and acetic anhydride form identical solutions in oleum solvents, provided that the stoicheiometrical compositions of the solutions are identical. The same conclusion may be drawn for benzoic acid and benzoic anhydride (Fig. 2, Table 5). The following demonstration of the mode of ionisation of acetic and benzoic acids in oleum will therefore apply also to the anhydrides.

Acetic and benzoic acids behave as monoacid bases in aqueous sulphuric acid. Similar behaviour in oleum would lead to expression (10), because the relative strengths of sulphuric acid and disulphuric acids are such that the equilibrium (11) lies to the right-hand side (Brand, *loc. cit.*; Gillespie, *J.*, 1950, 2516).

$$R{\cdot}CO_2H + H_2S_2O_7 = R{\cdot}CO_2H_2^+ + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$H_2S_2O_7 + HSO_4^- = HS_2O_7^- + H_2SO_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

In oleum solution, however, there is the possibility of ionisation (12) :

$$R{\cdot}CO_2H + 2H_2S_2O_7 = R{\cdot}CO^+ + HS_2O_7^- + 2H_2SO_4 \quad . \quad . \quad . \quad . \quad (12)$$

These two possibilities cannot be distinguished by direct determination of the *i*-factors because of complicating equilibria in the oleum solvent (Gillespie, *loc. cit.*); a comparative procedure was therefore employed, using the solute ammonium sulphate as a standard.

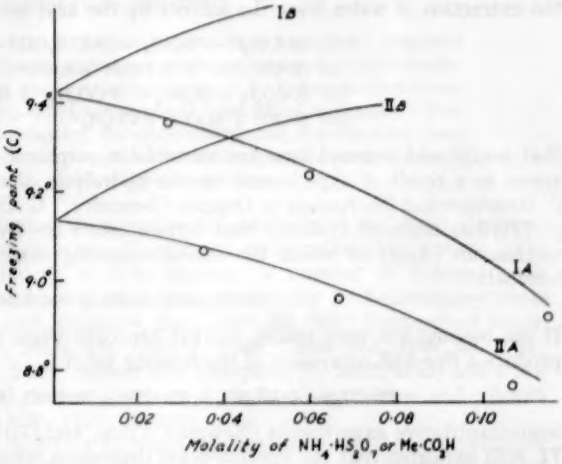


FIG. 3. *Freezing points of solutions of ammonium sulphate and acetic acid in oleum.*

Initial molality of $H_2S_2O_7$; I = 0·1420, II = 0·1822.

Added solute: A = $(NH_4)_2SO_4$, B = $(NH_4)_2SO_4 + H_2O$ (1 : 2). ○ = acetic acid (experimental points).

Fig. 3 shows the results of such a comparison, in two different oleum solvents, for the case of acetic acid. The curves A describe the change of f. p. when ammonium sulphate is added to oleum solvents. [Ammonium sulphate is expressed as ammonium hydrogen disulphate : see expression (13).] Ammonium sulphate ionises in oleum according to (13) (*idem, loc. cit.*).

$$\tfrac{1}{2}(NH_4)_2SO_4 + H_2S_2O_7 = NH_4^+ + HS_2O_7^- + \tfrac{1}{2}H_2SO_4 \quad . \quad . \quad . \quad . \quad (13)$$

This equation is cryoscopically similar to (10), if we neglect the small diluting effect of the sulphuric acid formed in reaction (13). The curves B show the change of f. p. when the solute is a mixture of ammonium sulphate and water in the molecular ratio of 1 : 2.

$$[\tfrac{1}{2}(NH_4)_2SO_4 + H_2O] + 2H_2S_2O_7 = NH_4^+ + HS_2O_7^- + 2\tfrac{1}{2}H_2SO_4 \quad . \quad . \quad . \quad . \quad (14)$$

Expression (14) is cryoscopically similar to (12), the effect of the sulphuric acid formed being again neglected. Comparison of the experimental points with the curves indicates that acetic acid ionises in oleum solutions according to equation (10) and not according to (12); the fact that the points do not exactly coincide with the curves A may be attributed to small differences in the cryoscopic properties of the ammonium and the acetic acidium ions. The possibility that a small but cryoscopically significant proportion of acetic acid ionises according to expression (12) can be discounted by a comparison of the results for the two oleum solvents. For if reaction (12) were significant in the weaker oleum (I) we should expect it to be more prominent in the

stronger oleum (*II*): the experimental points should then be further below curve *A* in the case of *I* than in the case of *II*. This is the opposite of what is observed. Qualitatively similar results are obtained with benzoic acid, but the experimental points lie somewhat further below the curves than with acetic acid.

The derivation of the curves in Fig. 3 is similar to that in Figs. 1 and 2. It is necessary to find the f. p.s of certain mixtures of ammonium sulphate, disulphuric acid, and sulphuric acid: this was done by interpolation, with Gillespie's data on the f. p. of solutions of disulphuric acid in sulphuric acid (*J.*, 1950, 2493), and of ammonium sulphate in oleum solvents (*ibid.*, p. 2516, Table 1, Expts. 10 and 104), supplemented by the results in Table 6. The acetic and benzoic acid results are in Tables 4 and 5.

It has now been shown that acetic and benzoic acids and anhydrides dissolve, both in dilute oleums and in aqueous sulphuric acid, to give carboxylic acidium ions. It is therefore concluded that similar behaviour occurs in 100% sulphuric acid, and that the ionisation of the anhydrides in this solvent is given by expression (3).

Discussion

The mechanism of the hydrolysis of acetic and benzoic anhydride by sulphuric acid is probably that suggested by Gillespie (*J.*, 1950, 2997), but with an additional stage (iv), the extraction of water from the solvent by the acyl ion. This stage (iv), which implies

(i) $(R{\cdot}CO)_2O + H_2SO_4 = (R{\cdot}CO)_2OH^+ + HSO_4^-$
(ii) $(R{\cdot}CO)_2OH^+ = R{\cdot}CO_2H + R{\cdot}CO^+$
(iii) $R{\cdot}CO_2H + H_2SO_4 = R{\cdot}CO_2H_2^+ + HSO_4^-$
(iv) $R{\cdot}CO^+ + H_2O = R{\cdot}CO_2H_2^+$

that acetyl and benzoyl ions are unstable in sulphuric acid, solves a problem that has arisen as a result of experiments on the hydrolysis of esters by sulphuric acid. Ingold ("Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 771) has adduced evidence that certain esters are hydrolysed in sulphuric acid by a mechanism ($A_{AC}1$) of which the rate-determining stage is, for the example of methyl benzoate:

$$Ph{\cdot}CO_2MeH^+ = Ph{\cdot}CO^+ + MeOH$$

If the benzoyl ion were stable, methyl benzoate when fully "hydrolysed" should thus produce a five-fold depression of the freezing point:

$$Ph{\cdot}CO_2Me + 3H_2SO_4 = Ph{\cdot}CO^+ + MeHSO_4 + H_3O^+ + 2HSO_4^-$$

Semiquantitative experiments (Newman, Craig, and Garnett, *J. Amer. Chem. Soc.*, 1949, **71**, 869) indicated that the freezing-point depression corresponding to complete hydrolysis is in fact only three-fold. This result, which has been confirmed quantitatively (Leisten, unpublished experiments), leads to the conclusion that the hydrolysis produces the benzoic acidium ion:

$$Ph{\cdot}CO_2Me + 2H_2SO_4 = Ph{\cdot}CO_2H_2^+ + MeSO_4H + HSO_4^-$$

The apparent contradiction between this conclusion, the then accepted stability of the benzoyl ion, and the $A_{AC}1$ mechanism, led to the suggestion of an alternative mechanism (Gillespie and Leisten, *Quart. Reviews*, 1954, **8**, 40); the acceptance of stage (iv), however, removes this objection to the $A_{AC}1$ mechanism, and the alternative mechanism now appears improbable. The mechanism for the hydrolysis of certain esters put forward by Kuhn and Corwin (*J. Amer. Chem. Soc.*, 1948, **70**, 3370) also appears improbable in the light of the present work, for it supposes the existence in sulphuric acid of acyl hydrogen sulphate molecules.

The demonstration that the acetyl and benzoyl ions do not exist in cryoscopically detectable amounts in sulphuric acid or in dilute oleum, is without prejudice to the existence of these ions in other systems, or as reaction intermediates. In fact the volume of evidence for these acetyl ions (see Gillespie, *loc. cit.*) suggests that the equilibrium $R{\cdot}CO_2H_2^+ + H_2S_2O_7 \rightleftharpoons R{\cdot}CO^+ + 2H_2SO_4$ is a significant one, and that by increasing the proportion of disulphuric acid to sulphuric acid in solutions of the anhydrides, the

acidium ions could be converted into the acyl ions. This conversion, which might be detected spectroscopically, appears more probable when it is considered that certain acids (*e.g.*, mesitoic acid) are known to form acyl ions in aqueous sulphuric acid, and that others (*e.g.*, 3 : 5-dibromo-2 : 4 : 6-trimethylbenzoic acid) probably yield a mixture of acyl and acidium ions in the same solvent (Treffers and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 1758).

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Polyazanaphthalenes. Part I. Some Derivatives of 1 : 4 : 5-*Triazanaphthalene and Quinoxaline.*

By C. L. LEESE and H. N. RYDON.

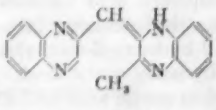
[Reprint Order No. 5770.]

Numerous derivatives of 1 : 4 : 5-triazanaphthalene have been prepared by condensation of 2 : 3-diaminopyridines with α-diketones, ethyl oxaloacetate and ethyl pyruvate, and by condensation of 2 : 6-diamino-3-nitrosopyridine with deoxybenzoin, ethyl acetoacetate, and ethyl malonate. Two analogues of pteroic acid containing the quinoxaline ring system have been synthesised. An orange compound similar to methylpteridine-red has been obtained by the action of acid on 2-methylquinoxaline.

THE work described in this paper had as its objective the synthesis of analogues of pteroic acid based on the 1 : 4 : 5-triazanaphthalene (I) and the quinoxaline ring system. The chemistry of 1 : 4 : 5-triazanaphthalene is little known; a number of symmetrically 2 : 3-disubstituted derivatives have been prepared by condensing 2 : 3-diaminopyridines with α-diketones (Tschitschibabin and Kirsanow, *Ber.*, 1927, **60**, 766; Petrow and Saper, *J.*, 1948, 1389; Bernstein, Stearns, Shaw, and Lott, *J. Amer. Chem. Soc.*, 1947, **69**, 1151; Lappin and Slezak, *ibid.*, 1950, **72**, 2806; Albert and Hampton, *J.*, 1952, 4985) and a few unsymmetrically 2 : 3-disubstituted derivatives from 2 : 3-diaminopyridines and alloxan (Rudy and Majer, *Ber.*, 1938, **71**, 1323; 1939, **72**, 940).

Petrow and Saper (*loc. cit.*) obtained 1 : 4 : 5-triazanaphthalene itself (I) in poor yield by condensation of 2 : 3-diaminopyridine with glyoxal; we have obtained a greatly improved yield by this method and have also obtained this compound by hydrogenolysis of the 7-bromo-derivative. We have also prepared 7-chloro-, 7-chloro-2 : 3-dimethyl-, and 7-chloro-2 : 3-diphenyl-1 : 4 : 5-triazanaphthalene by condensing 2 : 3-diamino-5-chloropyridine with the appropriate α-dicarbonyl compound.

(I)

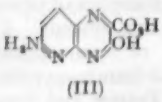
 (II)

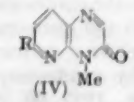
Attempts to prepare 2- or 3-methyl-1 : 4 : 5-triazanaphthalene by condensing 2 : 3-diaminopyridine with pyruvic aldehyde or hydroxyiminoacetone yielded intractable red pigments. This is surprising since *o*-phenylenediamine condenses readily with pyruvic aldehyde (Jones, Kornfeld, and McLaughlin, *J. Amer. Chem. Soc.*, 1950, **72**, 3539) and hydroxyiminoacetone (Böttcher, *Ber.*, 1913, **46**, 3084; Bennett and Willis, *J.*, 1928, 1960; Borsche and Doeller, *Annalen*, 1939, **537**, 39) to yield 2-methylquinoxaline and with dimethylglyoxime to yield 2 : 3-dimethylquinoxaline. An orange pigment, "2-methylquinoxaline-orange," is formed as a by-product in the condensation of *o*-phenylenediamine with hydroxyiminoacetone in aqueous hydrochloric acid and is also produced by the action

of aqueous hydrochloric acid on 2-methylquinoxaline; this compound we formulate as (II), by analogy with " methylpteridine-red " (Karrer, Schwyzer, and Nicolaus, *Helv. Chim. Acta*, 1950, **33**, 557, 1233). The red compounds produced from 2 : 3-diaminopyridine no doubt have similar structures. Attempts to condense 2 : 3-diaminopyridine, or its 5-chloro- or 5-bromo-derivative with pyruvic aldehyde di-*n*-butyl acetal, $\alpha\alpha'$-dichloroacetone, ethyl $\alpha\beta$-dibromopropionate, dihydroxyacetone, and hexoses likewise failed, as did attempted condensation of 2 : 3-diaminopyridine with $\alpha\beta$-dibromopropaldehyde and *p*-aminobenzoic acid (cf. the synthesis of pteroic acid; Waller *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 19).

Timmis (*Nature*, 1949, **164**, 139) prepared pteridines by condensing 4-amino-5-nitrosopyrimidines with suitably activated carbonyl compounds. Under the acid conditions employed by him, this reaction failed with 2 : 6-diamino-3-nitrosopyridine, yielding only black amorphous products; satisfactory results were, however, obtained on using ethanolic sodium ethoxide as the condensing agent. Thus, 2 : 6-diamino-3-nitrosopyridine and deoxybenzoin yielded 6-amino-2 : 3-diphenyl-1 : 4 : 5-triazanaphthalene, which was smoothly deaminated by nitrous acid to the corresponding 6-hydroxy-compound. Condensation of 2 : 6-diamino-3-nitrosopyridine with ethyl acetoacetate and ethyl malonate proceeded equally smoothly, affording 2-acetyl-6-amino-3-hydroxy-1 : 4 : 5-triazanaphthalene and 6-amino-3-hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxylic acid (III), respectively.

When heated, the acid (III) was smoothly decarboxylated to 6-amino-3-hydroxy-1 : 4 : 5-triazanaphthalene; this was readily methylated by methyl sulphate in alkaline solution to a compound formulated, by analogy with the quinoxaline series (for references see Simpson, " Condensed Pyridazine and Pyrazine Rings," Interscience Publ., New York, 1953, p. 241), as the *N*-methyl derivative (IV; R = NH_2), which yielded the corresponding 6-hydroxy-compound (IV; R = OH) on deamination.


(III)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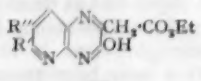
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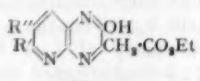
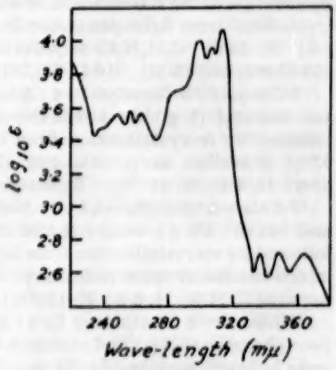

(VI)

We next investigated the applicability to the 1 : 4 : 5-triazanaphthalene series of the convenient procedure of Tschesche, Köhncke, and Korta (*Z. Naturforsch.*, 1950, **5b**, 132) for the synthesis of 7-hydroxypteridines. 2 : 3-Diamino-5-bromopyridine condensed smoothly with ethyl oxaloacetate in acetic acid to give the ester (V; R′ = H, R″ = Br), which was readily hydrolysed and decarboxylated to 7-bromo-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene, also obtained by condensation of 2 : 3-diamino-5-bromopyridine with ethyl pyruvate in benzene; hydrogenolysis yielded 3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene, likewise also obtained by condensing 2 : 3-diaminopyridine with ethyl pyruvate. A similar series of reactions with 2 : 3 : 6-triaminopyridine yielded the ester (V; R′ = NH_2, R″ = H) and 6-amino-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene. Substitution of 2N-sulphuric acid for acetic acid in the condensation of 2 : 3-diamino-5-bromopyridine with ethyl oxaloacetate led, after hydrolysis, decarboxylation, and hydrogenolysis to 2-hydroxy-3-methyl-1 : 4 : 5-triazanaphthalene, isomeric with the compound obtained by using acetic acid; the assignment of structure (V) to the condensation product formed in acetic acid and structure (VI) to that formed in sulphuric acid is based on similar findings in the pteridine field (cf. Elion, Hitchings, and Russell, *J. Amer. Chem. Soc.*, 1950, **72**, 78); an attempt to establish the structure of the ester (V; R′ = NH_2, R″ = H) by oxidising the derived amino-hydroxy-methyltriazanaphthalene to (III) with permanganate failed owing to breakdown of the ring-system with liberation of ammonia. Numerous attempts were made to brominate 3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene in the side-chain, but no homogeneous bromomethyl compound could be obtained; condensation of the crude bromination product with *p*-aminobenzoic acid gave none of the required pteroic acid analogue.

In general, derivatives of 1 : 4 : 5-triazanaphthalene appear to be less stable than their

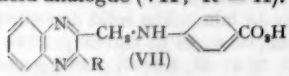
quinoxaline and pteridine analogues being, in many cases, very sensitive to both acid and alkali; as in the acridine (Albert, " The Acridines," Ed. Arnold, London, 1951, p. 152) and pteridine (Albert, Brown, and Cheeseman, *J.*, 1951, 474) series, and no doubt for the same reasons, the introduction of amino- or hydroxy-groups causes a marked lowering in solubility and increase in melting point.

The light absorption of 1 : 4 : 5-triazanaphthalene is shown in the Figure, while the rounded maxima for the two main peaks are compared with those for naphthalene and a series of azanaphthalenes in the Table. It will be seen that, except for quinoxaline, the successive replacement of methine by aza-groups leads to a progressive shortening of the wave-length of the maxima, the effect being greatest with the band of shorter wave-length; the reason for the irregularity with quinoxaline is obscure. Light-absorption data for the other 1 : 4 : 5-triazanaphthalene and quinoxaline derivatives prepared are recorded in the Experimental section.



Light absorption of 1 : 4 : 5-*triazanaphthalene in ethanol.*

In the quinoxaline series we were able to prepare two analogues of pteroic acid. Quinoxaline-2-aldehyde, prepared by an improved method from 2-D-*arabo*-tetrahydroxybutylquinoxaline, condensed readily with *p*-toluidine and *p*-aminobenzoic acid to yield Schiff's bases; that from *p*-aminobenzoic acid gave, on hydrogenation, the pteroic acid analogue (VII; R = H). 3-Hydroxy-2-methylquinoxaline was readily prepared from *o*-phenylenediamine and ethyl pyruvate, a method which is much superior to the older one employing pyruvic acid (Hinsberg, *Annalen*, 1896, **292**, 249); bromination afforded the 2-bromomethyl compound which with ethyl *p*-aminobenzoate gave a product which was readily hydrolysed to the pteroic acid analogue (VII; R = OH).



(VII)

Main absorption bands of naphthalene and some azanaphthalenes.

Compound	Solvent	$\lambda_{max.}$ (mμ)	$\log_{10}\varepsilon$	$\lambda_{max.}$ (mμ)	$\log_{10}\varepsilon$	Ref.
Naphthalene	EtOH	275	3·75	314	2·50	1
Quinoline	EtOH	276	3·59	313	3·41	2
Quinoxaline	MeOH	233	4·41	315	3·79	3
1 : 8-Naphthyridine	H_2O	260	3·62	305	3·81	4
1 : 4 : 7-Triazanaphthalene	EtOH	256	3·58	306	4·07	5
Pteridine	H_2O	234	3·50	304	3·87	4

1, Braude, *Ann. Reports*, 1945, **42**, 123. 2, Miller, Knight, and Roe, *J. Amer. Chem. Soc.*, 1950, **72**, 1629. 3, Bohlmann, *Chem. Ber.*, 1951, **84**, 860; Albert *et al.* (ref. 4) obtained almost identical results in water. 4, Albert, Brown, and Cheeseman, *J.*, 1951, 474. 5, This paper.

Experimental

Figures for light absorption are wave-lengths in mμ for maxima or inflections (in italics) and are followed by $\log_{10}\varepsilon$ in parentheses.

1 : 4 : 5-*Triazanaphthalene derivatives.*

1 : 4 : 5-*Triazanaphthalene.*—(*a*) 2 : 3-Diaminopyridine (0·5 g.) and glyoxal sodium bisulphite (1·33 g.) were refluxed in 50% aqueous ethanol (7 ml.) for 1 hr. The cooled mixture was made strongly alkaline with 5N-sodium hydroxide and continuously extracted with light petroleum (b. p. 40—60°) for 4 hr. The extract, after treatment with charcoal and filtration, deposited the base (0·3 g., 51%) as needles, m. p. 146° (Petrow and Saper, *loc. cit.*, give m. p. 147—148°); light absorption in EtOH, *238* (3·47), 249 (3·57), 256 (3·58), 263 (3·57), *286* (3·71), 299 (4·01), 306 (3·96), 313 (4·07), 337 (2·72), 348 (2·72), 364 (2·72).

(*b*) 7-Bromo-1 : 4 : 5-triazanaphthalene (2 g.; Petrow and Saper, *loc. cit.*) was suspended in 0·5N-sodium hydroxide and hydrogenated over 5% palladised strontium carbonate. After the theoretical amount of hydrogen had been absorbed, the solution was made more strongly

alkaline and continuously extracted with light petroleum (b. p. 60—80°) for 12 hr. The extract, after treatment with charcoal and filtration, deposited the base (0·51 g., 41%), m. p. 146°.

7-Chloro-1 : 4 : 5-triazanaphthalene.—2 : 3-Diamino-5-chloropyridine (1·43 g.) and glyoxal sodium bisulphite (2·6 g.) were heated in 25% aqueous ethanol (40 ml.) at 100° for 1 hr. Basification of the cooled solution with 5N-sodium hydroxide yielded the *base* (1·0 g., 60%) which crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 161° (Found : C, 50·6; H, 2·6; N, 25·6. $C_7H_4N_3Cl$ requires C, 50·8; H, 2·4; N, 25·4%); light absorption in EtOH, 258 (3·30), 265 (3·32), 310 (3·93), 316 (3·93), 324 (4·08).

7-Chloro-2 : 3-dimethyl-1 : 4 : 5-triazanaphthalene.—2 : 3-Diamino-5-chloropyridine (1·43 g.) and diacetyl (1 g.) were refluxed in ethanol (40 ml.) for 90 min. Evaporation to dryness, followed by recrystallisation from light petroleum (b. p. 80—100°), afforded the *base* (1·8 g., 93%) in needles, m. p. 155—156° (Found : C, 55·4; H, 4·2; N, 21·5. $C_9H_8N_3Cl$ requires C, 55·8; H, 4·1; N, 21·7%); light absorption in EtOH, 255 (3·43), 265 (3·32), 319 (4·09), 329 (4·16).

7-Chloro-2 : 3-diphenyl-1 : 4 : 5-triazanaphthalene.—2 : 3-Diamino-5-chloropyridine (1·43 g.) and benzil (2·1 g.) were refluxed in benzene (40 ml.) for 90 min. Evaporation to dryness, followed by recrystallisation from light petroleum (b. p. 80—100°), afforded the *base* (2·1 g., 66%) in fine needles or stout rods, m. p. 136—137° (Found : C, 71·5; H, 4·05; N, 13·1. $C_{19}H_{12}N_3Cl$ requires C, 71·8; H, 3·8; N, 13·2%); light absorption in EtOH, 228 (4·55), 236 (4·55), 364 (4·17).

6-Hydroxy-2 : 3-diphenyl-1 : 4 : 5-triazanaphthalene.—2 : 6-Diamino-3-nitrosopyridine (5 g.), deoxybenzoin (6·5 g.) and ethanolic sodium ethoxide (from sodium, 0·8 g., and ethanol, 150 ml.) were refluxed together for 24 hr. Recrystallisation, from ethanol, of the solid (6·5 g.) which separated from the cooled, filtered product yielded 6-amino-2 : 3-diphenyl-1 : 4 : 5-triazanaphthalene (4·1 g., 38%) as bright yellow needles, m. p. 271°, not depressed on admixture with a specimen prepared by Petrow and Saper's method (*loc. cit.*); light absorption in EtOH, 237 (4·64), 281 (4·13), 291 (4·13), 390 (4·38).

This amine (1·47 g.) was dissolved in warm 7N-sulphuric acid (50 ml.), and the solution cooled in ice; a solution of sodium nitrite (5 g.) in water (20 ml.) was added dropwise, with stirring, during 5 min. and the mixture then warmed at 100° for 15 min. The solid deposited on cooling was recrystallised from ethanol; the *hydroxy-compound* (1·0 g., 68%) had m. p. 273—274° (Found : C, 75·7; H, 4·5; N, 13·7. $C_{19}H_{13}ON_3$ requires C, 76·3; H, 4·3; N, 14·0%) and light absorption in EtOH, 280 (4·04), 290 (4·04), 376 (4·35).

2-Acetyl-6-amino-3-hydroxy-1 : 4 : 5-triazanaphthalene.—2 : 6-Diamino-3-nitrosopyridine (1·38 g.) was refluxed for 24 hr. with ethanolic ethyl sodioacetoacetate [from sodium, (0·23 g.), ethanol (50 ml.), and ethyl acetoacetate (1·3 g.)]. The brown solid which separated on cooling was collected, washed and dissolved in 0·01N-sodium hydroxide (50 ml.). After being heated with charcoal and filtered, the hot solution was acidified with 2N-hydrochloric acid. The *compound* (0·65 g., 32%) was a bright yellow granular solid, m. p. >360° (Found : C, 52·35; H, 4·1; N, 27·7. $C_9H_8O_2N_4$ requires C, 52·9; H, 3·9; N, 27·5%); light absorption in 0·01N-NaOH, 229 (4·40), 281 (3·73), 291 (3·80), 402 (416).

6-Amino-3-hydroxy-1 : 4 : 5-triazanaphthalene.—2 : 6-Diamino-3-nitrosopyridine (10 g.) was refluxed for 24 hr. with ethanolic ethyl sodiomalonate [from sodium (1·7 g.), ethanol (400 ml.), and ethyl malonate (12 g.)]. The mixture was then evaporated under reduced pressure and the residue dissolved in 0·2N-sodium hydroxide, heated with charcoal, filtered, and acidified while still hot with 2N-hydrochloric acid. *6-Amino-3-hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxylic acid* (III) (6·0 g., 40%) was precipitated as a bright yellow, granular powder, m. p. >360° (Found : C, 45·95; H, 3·4; N, 26·6. $C_8H_6O_3N_4$ requires C, 46·6; H, 2·9; N, 27·2%); light absorption in 0·01N-NaOH, 280 (3·46), 371 (4·05), *360* (3·98).

This acid (2 g.) was heated to above 300° in a nitrogen atmosphere at 20 mm. pressure. Resublimation of the sublimate afforded *6-amino-3-hydroxy-1 : 4 : 5-triazanaphthalene* (1 g., 63%) as fine yellow needles, m. p. >360° (Found : C, 51·9; H, 3·9; N, 35·1. $C_7H_6ON_4$ requires C, 51·8; H, 3·7; N, 34·6%); light absorption in 0·01N-NaOH, 280 (3·49), 352 (4·35), 367 (4·37). Methylation (methyl sulphate in N-sodium hydroxide), followed by recrystallisation from methanol, gave *6-amino-3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene* (IV; R = NH_2) (74%), m. p. 287—288° (Found : C, 55·1; H, 4·7; N, 31·2. $C_8H_8ON_4$ requires C, 54·5; H, 4·5; N, 31·8%); light absorption in EtOH, 369 (4·28). Sodium nitrite (0·26 g.) in water (5 ml.) was added dropwise to a stirred, ice-cooled solution of this *N*-methyl-compound (0·26 g.) in 2N-hydrochloric acid (50 ml.); the light brown precipitate was washed, dried, and recrystallised from *n*-butanol–light petroleum (b. p. 80—100°), affording *3 : 4-dihydro-6-hydroxy-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene* (IV; R = OH) (0·5 g., 83%), m. p. 297° (Found : C, 54·4; H, 4·3; N, 24·1. $C_8H_7O_2N_3$ requires C, 54·2; H, 3·9; N, 23·7%); light absorption in

EtOH, 227 (4·23), 347 (4·23), *354* (4·12); this compound resisted further methylation with methyl sulphate and aqueous sodium hydroxide.

7-Bromo-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene.—(*a*) 2 : 3-Diamino-5-bromopyridine (6·0 g.) in acetic acid (25 ml.) was mixed with ethyl sodio-oxaloacetate (8·75 g.) in acetic acid (50 ml.), and the mixture heated at 100° for 1 hr. The crystalline solid which separated (7·38 g., 74%), was washed, dried, and recrystallised from pyridine, affording *ethyl 7-bromo-3-hydroxy-1 : 4 : 5-triaza-2-naphthylacetate* (V; R′ = H, R″ = Br) in needles, decomp. 260° (Found: C, 41·9; H, 3·3; N, 12·8. $C_{11}H_{10}O_3N_3Br$ requires C, 42·3; H, 3·2; N, 13·5%); light absorption in EtOH, 281 (4·02), 290 (3·96), 360 (4·38). This ester (6·41 g.) was warmed with 2N-sodium hydroxide (25 ml.) for 30 min. The pH was brought to 8·5 with acetic acid, and the solution heated with charcoal and filtered; the pH of the filtrate was then brought to 4 with more acetic acid, carbon dioxide being copiously evolved. The precipitate was collected and recrystallised from ethanol, yielding *7-bromo-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene* (3·04 g., 62%), decomp. 240° (Found: C, 40·3; H, 2·6; N, 18·5. $C_8H_6ON_3Br$ requires C, 40·0; H, 2·5; N, 17·5%); light absorption in 0·01N-NaOH, 228 (4·52), 234 (4·44), 264 (3·92), *333* (4·10), 348 (4·14), *358* (4·10).

(*b*) The same compound was prepared by refluxing 2 : 3-diamino-5-bromopyridine (1·88 g.) and ethyl pyruvate (2·32 g.) in benzene (75 ml.) for 12 hr.; the pale brown precipitate was purified by acidification of its alkaline solution (yield, 1·22 g., 51%) (Found: C, 40·5; H, 2·7; N, 17·3%); light absorption in 0·01N-NaOH, 228 (4·53), 236 (4·45), 257 (3·89), 353 (4·13).

3-Hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene.—(*a*) 7-Bromo-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene (0·7 g.) was hydrogenated over 5% palladised strontium carbonate in 0·5N-sodium hydroxide (7 ml.). When absorption of hydrogen was complete, the solution was heated with charcoal, filtered, and acidified; vacuum-sublimation or crystallisation from ethanol yielded the *hydroxy-methyl-compound* (0·4 g., 85%) as needles, decomp. 240° (Found: C, 59·9; H, 4·6; N, 26·2. $C_8H_7ON_3$ requires C, 59·6; H, 4·3; N, 26·1%); light absorption in 0·01N-NaOH, 227 (4·44), 342 (4·10).

(*b*) The same compound was prepared by refluxing 2 : 3-diaminopyridine (0·7 g.) and ethyl pyruvate (0·8 g.) in benzene (25 ml.) for 1 hr. Vacuum-sublimation of the precipitate gave needles (0·6 g., 58%), decomp. 240° (Found: C, 59·9; H, 4·5%); light absorption in 0·01N-NaOH, 227 (4·32), 345 (4·12).

6-Amino-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene.—2 : 6-Diamino-3-nitrosopyridine (2·64 g.) was suspended in acetic acid (25 ml.) and hydrogenated over Adams catalyst. When the theoretical amount of hydrogen had been absorbed, ethyl sodio-oxaloacetate (5 g.) was added and the mixture heated on the steam-bath under nitrogen for 90 min. The crystalline precipitate was collected, washed with ethanol and ether, and recrystallised from pyridine, affording *ethyl 6-amino-3-hydroxy-1 : 4 : 5-triaza-2-naphthylacetate* (V; R′ = NH_2, R″ = H) (3·1 g., 66%), in yellow crystals, m. p. >360° (Found: C, 53·6; H, 4·9; N, 22·2. $C_{11}H_{13}O_3N_4$ requires C, 53·2; H, 4·8; N, 22·6%); light absorption in 0·01N-NaOH, 268 (3·38), 280 (3·40), 354 (4·36), 365 (4·36).

This ester (10 g.) was dissolved in 0·25N-sodium hydroxide (400 ml.), and the solution heated at 90° for 15 min. Acidification of the hot solution with acetic acid gave a gelatinous precipitate, which was collected by filtration, washed, dried, and sublimed in a high vacuum, yielding *6-amino-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene* (6 g., 85%) as colourless crystals, m. p. >360° (Found: C, 54·5; H, 4·7; N, 32·5. $C_6H_5ON_4$ requires C, 54·5; H, 4·5; N, 31·8%); light absorption in 0·01N-NaOH, 353 (4·33), 264 (4·33). Methylation (methyl sulphate in N-sodium hydroxide), followed by recrystallisation from aqueous methanol, afforded *6-amino-3 : 4-dihydro-2 : 4-dimethyl-3-oxo-1 : 4 : 5-triazanaphthalene* (74%), m. p. 296—297° (Found: C, 56·5; H, 5·4; N, 29·6. $C_9H_{10}ON_4$ requires C, 56·9; H, 5·3; N, 29·5%); light absorption in EtOH, 227 (4·30), 346 (4·22). This *N*-methyl-compound (0·4 g.) was dissolved in 4N-hydrochloric acid (15 ml.), and the solution cooled to 0° and treated dropwise with sodium nitrite (0·15 g.) in water (5 ml.); after 15 min. the crystalline precipitate was recrystallised from ethanol, affording *3 : 4-dihydro-6-hydroxy-2 : 4-dimethyl-3-oxo-1 : 4 : 5-triazanaphthalene* (0·2 g. 50%), m. p. 266—268° (Found: C, 56·1; H, 4·7; N, 21·8. $C_9H_9O_2N_3$ requires C, 56·6; H, 4·7; N, 22·0%); light absorption in EtOH, 342 (4·25).

2-Hydroxy-3-methyl-1 : 4 : 5-triazanaphthalene.—2 : 3-Diamino-5-bromopyridine (1·88 g.) and ethyl sodio-oxaloacetate (2·3 g.) were heated on the steam-bath in 2N-sulphuric acid (70 ml.) for 2 hr. The crystalline product was purified by acidification of its solution in dilute sodium hydroxide; this ester had light absorption in 0·01N-NaOH, 238 (4·38), 348 (4·16), *356* (4·10). Without further purification the ester (0·7 g.) was dissolved in N-sodium hydroxide (20 ml.) and

hydrogenated over 5% palladised strontium carbonate. Removal of the catalyst and acidification of the filtrate afforded the *hydroxy-methyl-compound*, decomp. 270° (Found: C, 59·9; H, 4·6; N, 26·2. $C_9H_7ON_3$ requires C, 59·6; N, 4·3; N, 26·1%); light absorption in 0·01N-NaOH, 343 (4·18).

Quinoxaline derivatives.

2-Methylquinoxaline and 2-Methylquinoxaline-orange.—*o*-Phenylenediamine (10 g.) and hydroxyiminoacetone (9 g.), in 2N-hydrochloric acid (50 ml.), were heated on the steam-bath for 20 min.; a deep red colour developed after 2 min. The solution was basified with sodium hydroxide, and the red amorphous precipitate removed by filtration and recrystallised from ethyl acetate; "*2-methylquinoxaline-orange*" (II) (0·8 g., 6%) formed orange needles, m. p. 255° (Found: C, 75·9; H, 4·6; N, 19·5. $C_{18}H_{14}N_4$ requires C, 75·5; H, 4·9; N, 19·6%); light absorption in EtOH, *225* (4·61), 271 (4·71), 278 (4·71), 369 (4·24), 382 (4·24), 455 (3·76), 484 (3·80). Extraction of the filtrate with ether, followed by distillation of the dried extract, yielded 2-methylquinoxaline (10·1 g., 76%), b. p. 110—111°/15 mm.

2 : 3-Dimethylquinoxaline.—*o*-Phenylenediamine (2 g.) and dimethylglyoxime (2 g.) in 2N-hydrochloric acid (25 ml.) were heated on the steam-bath for 1 hr. The product was treated with charcoal, filtered, and basified. Recrystallisation from hot water yielded 2 : 3-dimethylquinoxaline (2·6 g., 89%), m. p. 104—105°.

Quinoxaline-2-aldehyde and its Derivatives.—2-D-*arabo*-Tetrahydroxybutylquinoxaline (5 g.; Ohle and Hielscher, *Ber.*, 1941, **74**, 13) and sodium metaperiodate (13 g.) were suspended in water (300 ml.), containing acetic acid (10 ml.). After 16 hr. at room temperature with occasional shaking, the mixture was filtered and the filtrate continuously extracted with ether for 4 hr. Evaporation of the dried extract afforded the aldehyde (2 g., 63%), pale yellow needles (from light petroleum), m. p. 107—108° (lit., m. p. 108°); light absorption in EtOH, 235 (4·49), *304* (3·79), 314 (3·85).

The aldehyde (0·25 g.), in ethanol (5 ml.) was added to a boiling solution of *p*-toluidine (0·5 g.) in water (30 ml.), containing acetic acid (2 ml.), sodium acetate (1 g.), and sodium hydrogen carbonate (0·05 g.). After 5 minutes' heating, the mixture was diluted with water (20 ml.) and cooled. Recrystallisation of the precipitate from aqueous ethanol or from methanol yielded N-*2'-quinoxalinylmethylene*-p-*toluidine* (0·37 g., 95%), as orange prisms or needles, m. p. 120—121° (Found: C, 77·8; H, 5·3; N, 17·5. $C_{16}H_{13}N_3$ requires C, 77·7; H, 5·3; N, 17·0%); light absorption in EtOH, 227 (4·32), *247* (4·40), 251 (4·44), *256* (4·40), *333* (4·24), 348 (4·27).

The aldehyde (1 g.) in ethanol (10 ml.), was condensed similarly with *p*-aminobenzoic acid (2·6 g.), in acetic acid (5 ml.) and water (200 ml.), containing sodium acetate (10 g.) and sodium hydrogen carbonate (0·5 g.). Crystallisation of the solid product from ethanol–pyridine yielded N-*2'-quinoxalinylmethylene*-p-*aminobenzoic acid* (1·6 g., 91%), as pale yellow needles, m. p. 288° (Found: C, 69·9; H, 4·6; N, 15·4. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·2%); light absorption in EtOH, 227 (4·50), 286 (4·50), 290 (4·50). This Schiff's base (1·0 g.) was hydrogenated over Adams catalyst (0·01 g.) in ethanol (250 ml.). When hydrogen-uptake ceased, the deep red solution was boiled with charcoal, filtered, concentrated under reduced pressure to 30 ml., and diluted with water (100 ml.). The light brown precipitate which was slowly formed was purified by precipitation with acetic acid from its solution in dilute aqueous ammonia; N-*2'-quinoxalinylmethyl*-p-*aminobenzoic acid* (VII; R = H) was so obtained as a pale brown amorphous solid melting indefinitely between 160° and 190° (Found: C, 69·0; H, 5·0; N, 15·1. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%); light absorption in EtOH, 237 (4·42), 251 (4·16), 257 (4·16), 268 (4·24), 291 (4·16), 314 (3·90).

3-Hydroxy-2-methylquinoxaline and its Derivatives.—*o*-Phenylenediamine (20 g.) in benzene (200 ml.) was treated with ethyl pyruvate (20 g.); after the vigorous reaction, which necessitated cooling, had abated, the crude 3-hydroxy-2-methylquinoxaline was collected and recrystallised from aqueous ethanol (yield, 24 g., 76%; m. p. 245—246°; lit., m. p. 245°); light absorption in 0·01N-NaOH, 237 (4·42), 343 (3·85). This compound (6·4 g.) and anhydrous sodium acetate (2·8 g.) were dissolved in warm acetic acid (120 ml.); a solution of bromine (6·2 g.) in acetic acid (20 ml.) was added gradually, with stirring, and the mixture heated on the steam-bath for 15 min. The crystals, which separated on cooling, were collected by filtration (7·1 g., 75%); sublimation at 4×10^{-4} mm. yielded *2-bromomethyl-3-hydroxyquinoxaline*, decomp. 225° (Found: C, 45·3; H, 3·5; Br, 33·35. $C_9H_7ON_2Br$ requires C, 45·3; H, 2·95; Br, 33·4%), characterised as the quaternary *pyridinium bromide*, needles (from ethanol), m. p. 244—245° (Found: C, 52·6; H, 4·05; Br, 24·6. $C_{14}H_{12}ON_3Br$ requires C, 52·85; N, 3·8; Br, 25·1%).

The bromomethyl compound (1 g.), ethyl *p*-aminobenzoate (0·7 g.) and calcium carbonate (0·45 g.) were refluxed in ethanol (100 ml.) for 4 hr. The filtered solution was diluted with water (200 ml.), and the pale brown precipitate which slowly formed was reprecipitated from its solution in dilute sodium hydroxide solution by acidification with acetic acid. The resulting *N-(3-hydroxy-2-quinoxalinylmethyl)-p-aminobenzoic acid* (VII; R = OH) was a light brown solid, decomp. 200° (Found: C, 64·2; H, 4·35; N, 14·7. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%); light absorption in 0·01N-NaOH, 227 (4·46), 236 (4·46), 328 (3·93), 348 (4·05), 358 (4·00).

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Synthetic Experiments in the cyclo*Heptatrienone Series. Part V.* Some Derivatives of 4-Hydroxytropone.*

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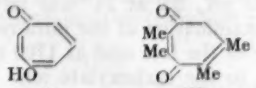
[Reprint Order No. 5782.]

Attempts are described to degrade tropone-4-carboxylic acid and its derivatives to 4-hydroxytropone. The Buchner ring-expansion of quinol dimethyl ether and subsequent oxidation by bromine lead either to 4-hydroxytropone-6-carboxylic acid or to a dibromo-4-hydroxytropone.

IN a study of the simple 3- and 4-substituted tropones, the synthesis of 3- and 4-hydroxytropone is essential because of their obvious relation to tropolone. 3-Hydroxytropone has been prepared recently (Part IV *), and preliminary attempts to synthesise 4-hydroxytropone (I) will be discussed in the present paper. Except for 5-hydroxytropolone and certain of its substitution products which in their behaviour are essentially substituted tropolones rather than tropones, a few compounds related to (I) have been described in the literature. Duroquinone and diazomethane have been reported (Smith and Pings, *J. Org. Chem.*, 1937, **2**, 95) to give some of a compound (II) which, as its monoenol, would be 4-hydroxy-2 : 3 : 6 : 7-tetramethyltropone. In a rather similar investigation (Marini-Bettolo and Paolini, *Gazzetta*, 1954, **84**, 327) 2 : 6-dimethoxybenzoquinone with diazomethane was found to give a colourless product formulated as (III). Both of the structures (II) and (III) are open to criticism on the grounds of certain of the physical



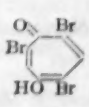
(I) (II) (III)

and chemical properties recorded and further study is necessary. Nozoe, Kitahara, and Abe (*Proc. Japan Acad.*, 1953, **29**, 347) were able to introduce a nuclear hydroxyl group into 2 : 4 : 7-tribromotropone by treatment with warm dilute sulphuric acid to give the compound (IV) but failed to remove the bromine atoms by hydrogenolysis without simultaneously reducing the ring. This behaviour contrasts with that of 2 : 4 : 7-tribromotropone which is an intermediate in the synthesis of tropone from *cyclo*hexenone or from *cyclo*hexanone (Dauben and Ringold, *J. Amer. Chem. Soc.*, 1951, **73**, 876; Nozoe, Kitahara, Ando, Masamune, and Abe, *Sci. Rep. Tôhoku Univ.*, 1952, **36**, 166) and with that of 2 : 5 : 7-tribromo-3-hydroxytropone, an intermediate in the synthesis of 3-hydroxytropone (Part IV). In a more detailed examination of the hydrogenolysis of 2 : 4 : 7-

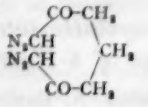
* Part IV, *J.*, 1954, 4605.

tribromotropone (Seto, *ibid.*, 1953, **37**, 377) 4-bromotropone has been isolated as a by-product (a small yield of 5-bromo-3-hydroxytropone was obtained as a by-product from the hydrogenolysis of 2 : 5 : 7-tribromo-3-hydroxytropone; Part IV) and, if this compound could be obtained in reasonable amounts, the hydrolysis to 4-hydroxytropone should present no difficulties. An attempt to convert 4-amino-7-phenyltropone into the 4-hydroxy-compound was unsuccessful (Nozoe, Mukai, and Minegishi, *Proc. Japan Acad.*, 1952, **28**, 287) and an uncharacterised yellow compound which gave no ketonic reactions and was possibly impure 4-hydroxytropone has been isolated from the reaction of 1 : 7-bisdiazoheptane-2 : 6-dione (V) with copper oxide (Rudolph and Hofmann, *Chem. Listy*, 1952, **45**, 261).

The synthesis of 4-hydroxy-2 : 3-benzotropone has been reported recently (Buchanan, *J.*, 1954, 1060; see also Barltrop, Johnson, and Meakins, *J.*, 1951, 181) and 4-hydroxy-5-phenyl-2 : 3 : 6 : 7-dibenzotropone (VI) is also known (Cook, *J.*, 1928, **58**; Buchanan, *Chem. and Ind.*, 1952, 855) but, as in the tropolone series, the fused benzenoid rings doubtless will exert a considerable effect on the behaviour of the hydroxytropone.



(IV)



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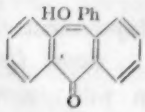
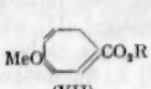
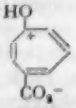


(VI)

An attractive possibility for the synthesis of 4-hydroxtyropone seemed to be the substitution of a hydroxyl for the carboxy-group in tropone-4-carboxylic acid. As has been shown (Bartels-Keith, Johnson, and Langemann, *J.*, 1952, 4461) this acid may be prepared conveniently by reaction of anisole and ethyl diazoacetate and, after hydrolysis of the product so obtained, phenoxyacetic acid and 4-methoxy*cyclo*hepta-1 : 3 : 5-trienecarboxylic acid (VII; R = H) have been isolated. The latter acid can then be oxidised to tropone-4-carboxylic acid with bromine. Later experiments have shown that the yield of the ester (VII; R = Et) is increased materially (to 58% calculated on ethyl diazoacetate) if the condensation is carried out in a glass-lined autoclave in an atmosphere of oxygen-free nitrogen (25 atm.) as recommended by Grundmann and Ottmann (*Annalen*, 1953, **582**, 163) for the similar reaction with benzene.



(VII)



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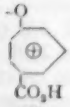


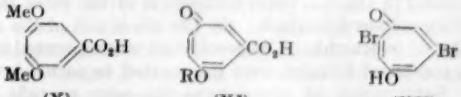
(IX)

Tropone-4-carboxylic acid, which has pK_a 3·2 at 24° was formerly believed to have the zwitterion structure (VIII) but an examination of the infra-red spectrum of its silver salt showed that the carbonyl frequency of the free acid at 1709 cm.$^{-1}$ had been replaced by a new band at 1555 cm.$^{-1}$ ascribed to the carboxylate ion. The carbonyl band at 1629 cm.$^{-1}$, corresponding to the tropone-carbonyl group, was unchanged. In methyl tropone-4-carboxylate, the ester-carbonyl band is at 1715 cm.$^{-1}$ and the tropone-carbonyl band at 1634 cm.$^{-1}$. The structure of the acid has therefore been amended to (IX), *i.e.*, that of a normal substituted tropone.

A number of attempts to degrade the carboxyl of (IX) to a hydroxyl, bromo-, or amino-group, had no success, including the Schmidt reaction on the free acid, the Curtius reaction on the acid chloride, and the action of bromine on the silver salt and on the free acid. The action of silver trifluoroacetate and bromine on the acid (VII; R = H) (cf. Rottenberg, *Helv. Chim. Acta*, 1953, **36**, 1115) and the Hofmann reaction on its amide gave tropone-4-carboxylic acid as the sole recognisable product. This approach has therefore been temporarily abandoned. In the course of the work several new derivatives of 4-methoxy-*cyclo*hepta-1 : 3 : 5-trienecarboxylic acid and of tropone-4-carboxylic acid were prepared but in general attempts to prepare derivatives of the acid (IX) from the corresponding

derivatives of (VII; R = H) were unsuccessful and led to the production of tropone-4-carboxylic acid itself. With excess of bromine the acid (IX) gave a dibromo-substitution product and, in a further structural proof, the acid has been treated with hydroxylamine (cf. Nozoe, Kitahara, Ando, Masamune, and Abe, *loc. cit.*) to give 2-aminotropone-5-carboxylic acid, which by reaction with alkali gave the known tropolone-5-carboxylic acid (Cook, Raphael, and Scott, *J.*, 1952, 4416).

We therefore turned to the possibility of obtaining 4-hydroxytropone from quinol dimethyl ether by methods analogous to those used for the conversion of resorcinol dimethyl ether into 3-hydroxytropone (Part IV, *loc. cit.*). Application of the Buchner ring-expansion method to quinol dimethyl ether and subsequent hydrolysis of the ester mixture gave 3 : 6-dimethoxy*cyclo*heptatrienecarboxylic acid (X or a double-bond isomer) as bright yellow needles, together with relatively high yields of *p*-methoxyphenoxyacetic acid (Johnson, Langemann, and Murray, *J.*, 1953, 2136). Oxidation of the product (X) with bromine (1 mol.) gave 4-methoxytropone-6-carboxylic acid (XI; R = Me) and hydrolysis of this acid gave 5-hydroxytropone-3-carboxylic acid (XI; R = H) as pale yellow needles which could be sublimed only with difficulty (cf. Johnson and Todd, Abs. 12th Int. Congr. I.U.P.A.C., 1951, p. 398). The structure of this acid was confirmed by the alkaline rearrangement of its methyl ether to 5-hydroxy*iso*phthalic acid. Despite numerous attempts however the acid (XI; R = H) could not be decarboxylated and in this respect is in line with the other troponecarboxylic acids.



(X) (XI) (XII)

Treatment of the acid (X) with larger quantities of bromine caused brominative decarboxylation, as in the 3-hydroxytropone series, and there was isolated a dibromo-4-hydroxytropone, possibly (XII), though in amount insufficient for structural determination. However, it appears that one of the bromine substituents must be in the 3-position, formerly occupied by the carboxyl group, and the other is probably in an α-position to the carbonyl, preference being given to (XII) on steric grounds. Experiments on decarboxylation of the dimethoxy-acid (X) and oxidation of the product are in progress.

In connection with the general formation of phenoxyacetic esters from the reaction of alkoxybenzenes with ethyl diazoacetate (Johnson, Langemann, and Murray, *loc. cit.*) it was of interest to find that a similar reaction occurred with dimethylaniline which gave *N*-methyl-*N*-phenylglycine ester together with an unidentified basic yellow liquid ester, the latter possibly being a product of ring expansion. The reaction of aliphatic diazo-compounds, R_2CN_2, with tertiary amines, $R'{\cdot}NMe_2$, is also known to give products of the type $R_2R'C{\cdot}NMe_2$ in certain cases (Bamford and Stevens, *J.*, 1952, 4675).

Experimental

Except where otherwise stated, ultra-violet absorption spectra have been determined in 95% ethanol and infra-red spectra determined as Nujol mulls.

4-Methoxycyclohepta-1 : 3 : 5-trienecarboxylic Acid and Derivatives (cf. Part II, *loc. cit.*).—Distilled anisole (580 g.) was treated with ethyl diazoacetate (32 g.; b. p. 38°/8 mm.) in a glass-lined autoclave at 160—165° for 5 hr. under oxygen-free nitrogen (25 atm.). At the end of the reaction the pressure had risen to 47 atm. The excess of anisole was removed at 100° under reduced pressure and the residual viscous brown oil distilled, giving (i) a pale yellow liquid, b. p. 99—111°/0·5 mm. (30·4 g., 58% calc. on ethyl diazoacetate), (ii) a viscous yellow liquid, b. p. 126—143°/0·5 mm. (5·3 g.), and (iii) residual brown tar (7·9 g.). Hydrolysis of fraction (i) (5 g) with methanolic potassium hydroxide gave 4-methoxy*cyclo*hepta-1 : 3 : 5-trienecarboxylic acid as described in Part II. The *methyl ester* was obtained from the acid (453 mg.) and ethereal diazomethane, as a light yellow oil (476 mg.; distilled at 0·2 mm.), n_D^{18} 1·5625 (Found: C, 66·8; H, 7·0. $C_{10}H_{12}O_3$ requires C, 66·65; H, 6·7%). Light absorption:

max. at 223—225 and 314—315 mμ (log ε 4·17 and 4·05 respectively). The *amide* was obtained by keeping a suspension of the methyl ester (752 mg.) in 35% aqueous ammonia (10 c.c.) for 3 weeks at room temperature with frequent shaking; the crystals were then separated (348 mg.) and washed with a little ether, and the filtrate extracted with ether (3 × 15 c.c.). Removal of the solvent from the dried extract gave a semi-crystalline product which was recrystallised from ether as colourless plates (279 mg.), m. p. 141—142°, which were combined with the first amount. For analysis a sample was sublimed at 125°/0·1 mm. (Found: C, 65·7; H, 7·0. $C_9H_{11}O_2N$ requires C, 65·45; H, 6·7%).

Derivatives of Tropone-4-carboxylic Acid.—Silver salt. The acid (3·7 g.; Part II) was suspended in water (20 c.c.) and neutralised to pH 7 with 4N-sodium hydroxide. A saturated aqueous solution of silver nitrate (4·6 g.) was added and the brown precipitate separated and crystallised from water to give the silver salt as pale yellow needles (4·29 g.). The infra-red spectrum showed max. at 1634, 1555, 1541, 1418, 1277, 1227, 1105, 1034, 952, 907, 876, 849, 819, 810, 801, 777, and 749 cm.$^{-1}$.

Methyl ester. (*a*) Tropone-4-carboxylic acid (767 mg.) was dissolved in dry methanol (50 c.c.) and pyridine (0·5 c.c.) and a solution of di*cyclo*hexylcarbodi-imide (Schmidt, Hitzler, and Lahde, *Ber.*, 1938, **71**, 1933) in dry ether (30 c.c.) was added. After 30 min. at room temperature the solvents were removed at reduced pressure and the light brown residue was extracted with hot ether (3 × 50 c.c.). Evaporation of the ether gave a brown semi-crystalline product which on sublimation at 67°/0·2 mm. gave the ester as colourless needles, m. p. 90° (Found: C, 65·8; H, 5·1. $C_9H_8O_3$ requires C, 65·85; H, 4·9%). The infra-red spectrum showed max. at 1715, 1634, 1610, 1587, 1435, 1364, 1277, 1227, 1214, 1186, 1111, 1083, 1030, 943, 899, 867, 847, 813, 800, and 773 cm.$^{-1}$. Recrystallisation of the ester from light petroleum (b. p. 40—60°) gave a slightly coloured product. (*b*) The silver salt of the acid (615 mg.) was shaken with methyl iodide (2 c.c.) overnight. The precipitate was separated and washed with methanol (3 × 2 c.c.) and the combined filtrates were evaporated *in vacuo*, leaving a light brown semi-crystalline residue. Sublimation as above gave the ester as pale yellow needles (41 mg.), m. p. and mixed m. p. 88°.

Dibromotropone-4-carboxylic Acid.—A solution of tropone-4-carboxylic acid (601 mg.) in glacial acetic acid (30 c.c.) was treated with bromine (0·85 c.c.), and the brown solution heated under reflux for 1 hr. Removal of the solvent *in vacuo* on the steam-bath gave a light yellow solid which on recrystallisation from benzene–*cyclo*hexane gave pale yellow needles (882 mg.), m. p. 182—183° (decomp.) (Found: C, 31·6; H, 1·7. $C_8H_4O_3Br_2$ requires C, 31·2; H, 1·3%).

2-Aminotropone-5-carboxylic Acid.—Tropone-4-carboxylic acid (634 mg.) was heated in ethanol (20 c.c.) under reflux for 15 min. with hydroxylamine hydrochloride (0·9 g.) and pyridine (3 c.c.). After cooling, the dark brown mixture deposited a yellow crystalline precipitate which was separated. Concentration of the mother-liquors gave a further amount of crystals, and the combined material was recrystallised from ethanol, to give the *amino-acid* as short yellow needles (587 mg.), m. p. 280—282° (decomp.), which gave a green ferric reaction (Found: C, 58·5; H, 4·5; N, 8·2. $C_8H_7O_3N$ requires C, 58·2; H, 4·3; N, 8·5%). The infra-red spectrum showed max. at 3279, 3155, 1704, 1647, 1616, 1585, 1355, 1280, 1224, 1156, 1087, 897, 866, 823, 761, and 745 cm.$^{-1}$.

Tropolone-5-carboxylic Acid.—A solution of the amino-acid (307 mg.) in 4N-sodium hydroxide (15 c.c.) was heated on the steam-bath. Ammonia was evolved and after 2 hr. the solution was cooled and acidified by careful addition of concentrated sulphuric acid (3 c.c.). The pale yellow precipitate was separated and dried (283 mg.). Crystallisation from acetic acid followed by sublimation in a high vacuum gave a pale yellow, anhydrous *tropolone-5-carboxylic acid*, m. p. 187° (sealed tube), which gave a green ferric reaction (Cook, Raphael, and Scott, *loc. cit.*, give m. p. 222—225° for the monohydrate) (Found: C, 58·05; H, 3·9. $C_8H_6O_4$ requires C, 57·8; H, 3·6%). The infra-red spectrum showed max. at 3125, 1698, 1618, 1570, 1550, 1497, 1418, 1321, 1295, 1230, 1205, 1072, 769, 751, 731, and 691 cm.$^{-1}$. Treatment of the acid (226 mg.) in ether with excess of diazomethane, evaporation, and sublimation of the solid residue in a high vacuum gave light yellow prisms of the methyl ether methyl ester (233 mg.), m. p. 185° (Cook, Raphael, and Scott, *loc. cit.*, give m. p. 184·5°) (Found: C, 61·65; H, 5·4. Calc. for $C_{10}H_{10}O_4$: C, 61·85; H, 5·2%). The infra-red spectrum showed max. at 1724, 1631, 1585, 1513, 1404, 1362, 1299, 1277, 1255, 1215, 1176, 1120, 1082, 974, 942, 892, 861, 817, 771, 722, and 696 cm.$^{-1}$.

3 : 6-*Dimethoxycyclo*heptatrienecarboxylic Acid (cf. Johnson, Langemann, and Murray, *loc. cit.*).—Quinol dimethyl ether (300 g.) was heated with ethyl diazoacetate at 150—155° for 5 hr., the product fractionated, and the fraction of b. p. 115—160°/0·2 mm. (30 g.) collected.

A portion of this fraction (5 g.) was cooled to 0° and mixed with a cooled solution of potassium hydroxide (3·3 g.) in 90% methanol (30 c.c.) with stirring. After 15 min. at 0°, the precipitated potassium *p*-methoxyphenoxyacetic acid (2·3 g.) was separated and washed with a little methanol. The filtrate was then heated at 60—70° for 2 hr. in order to complete hydrolysis of the ester and to reduce the volume of solution to 10—15 c.c. The solution was cooled (ice), water (50 c.c.) added, and then concentrated hydrochloric acid carefully (temperature of the solution held at 0°). It was preferable to induce crystallisation of the product by rubbing and scratching in the early stages of the precipitation. After the addition of a slight excess of hydrochloric acid (no further precipitation), the suspension was kept for a further hour at 0°. The bright yellow *dimethoxy-acid* (0·74 g.) was then separated, washed, and dried. It crystallised from benzene–*cyclo*hexane in yellow needles, m. p. 153—154° (previous softening), subliming at 140°/0·5 mm. (Found: C, 61·5; H, 6·2. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·1%). Light absorption: max. at 356—357 and 222 mμ (log ε 3·59 and 4·32 respectively).

5-Methoxytropone-3-carboxylic Acid.—A solution of bromine (0·3 c.c.) in carbon tetrachloride (3 c.c.) was added, with stirring, to a solution of 3 : 6-dimethoxy*cyclo*heptatrienecarboxylic acid (1 g.) in chloroform (10 c.c.) at 0°. The dark oily suspension was warmed at 60° on the water-bath for 5 min., hydrogen bromide being evolved. The mixture was cooled to 0°, the supernatant liquid decanted and discarded, and the dark oil dissolved in a little methanol. The solvent was then removed under reduced pressure, the residue cooled (ice), and partial solidification induced by scratching. Water (2 c.c.) was added, and the suspension well mixed and kept at 0° for 15 min. The precipitated solid was separated, washed, and crystallised from water (charcoal), the *monoether* (0·76 g.) being obtained as yellow needles, m. p. 190° (decomp.) (Found: C, 60·1; H, 4·6. $C_9H_8O_4$ requires C, 60·0; H, 4·45%). Light absorption: max. at 352—353 and 222 mμ (log ε 4·11 and 4·32 respectively).

5-Hydroxytropone-3-carboxylic Acid.—The foregoing methoxy-acid (0·15 g.) in 48% aqueous hydrobromic acid (4 c.c.) and water (1 c.c.) was heated at 100° for 3 hr. The solvent was removed, water (3 c.c.) added, the suspension cooled in ice for 15 min., and the precipitate (0·13 g.) separated and dried. Crystallisation of the product from water (charcoal) gave *5-hydroxytropone-3-carboxylic acid* as pale yellow needles, m. p. 240° (after charring) (Found: C, 58·0; H, 3·6. $C_8H_6O_4$ requires C, 57·8; H, 3·6%). The product gave no marked ferric reaction, nor was it coloured in alkaline solution. It sublimed only with difficulty. Light absorption: max. at 356—359 and 221—223 mμ (log ε 4·09 and 4·29 respectively). The infra-red spectrum showed max. at 2941—2703 (broad band), 1786, 1715, 1647, 1629, 1595, 1531, 1486, 1422, 1379, 1351, 1238, 1098, 962, 904, 893, 850, 815, 778, 760, and 706 cm.$^{-1}$.

Alkaline Rearrangement of 5-Methoxytropone-3-carboxylic Acid.—The acid (0·2 g.), potassium hydroxide (5 g.), and water (1 c.c.) were heated at 250° in nickel crucible for 10 min. The melt was dissolved in water (10 c.c.) and acidified with sulphuric acid. The precipitated potassium sulphate was separated, and the dark filtrate thoroughly extracted with ether (8 × 25 c.c.). The solvent was removed from the dried combined ethereal extract, and the solid residue crystallised from water to give colourless 5-hydroxy*iso*phthalic acid, needles, m. p. and mixed m. p. 299° after sublimation *in vacuo*.

Dibromo-4-hydroxytropone.—Bromine (0·8 c.c.) was added dropwise to a solution of 3 : 6-dimethoxy*cyclo*heptatrienecarboxylic acid (0·45 g.) in glacial acetic acid (8 c.c.) and water (1 c.c.) at 0°. The dark red solution was then kept at room temperature for ½ hr., diluted with water (25 c.c.) and kept at 0° for 36 hr. The solvent was removed, and the residue treated with water (5 c.c.) and cooled (ice). The precipitated oil slowly solidified; the solid was separated, washed, and crystallised from aqueous dioxan (charcoal). The *dibromo-compound* (0·1 g.) was then sublimed at 140°/0·6 mm. and recrystallised from aqueous ethanol, then having m. p. 188—189° (decomp.) (Found, on a freshly sublimed sample: C, 29·8; H, 1·6. $C_7H_4O_2Br_2$ requires C, 30·0; H, 1·45%). Light absorption: max. at 370 and 247 mμ (log ε 4·16 and 4·24 respectively), inflection at 386—388 mμ (log ε 4·12). The infra-red spectrum showed max. at 1626, 1538, 1299, 1274, 1250, 1153, 1124, 993, 951, 921, 846, 781, 761, and 724 cm.$^{-1}$.

Reaction of Dimethylaniline and Ethyl Diazoacetate.—Purified dimethylaniline (168 g.) was heated to 160° and ethyl diazoacetate (40 g.) added dropwise with stirring during 2 hr. After *ca.* 15 min. a steady stream of nitrogen was evolved and after all the ethyl diazoacetate had been added the mixture was heated for a further hour. The excess of dimethylaniline was removed under reduced pressure, the residual dark yellow oil distilled, and the fraction of b. p. 117—142°/1 mm. (25·2 g.), a deep yellow oil, was collected. A portion (2·1 g.) of this fraction was shaken with aqueous ammonia (*d* 0·88; 8 c.c.) for 3 weeks and the crystalline product separated and recrystallised from aqueous methanol, to give colourless plates (214 mg.),

m. p. 162° alone and mixed with an authentic specimen of the amide of *N*-methyl-*N*-phenylglycine (Found: C, 65·8; H, 7·5; N, 17·2. Calc. for $C_9H_{11}ON_2$: C, 65·8; H, 7·4; N, 17·05%). No other pure compound has so far been isolated from the product.

Grateful acknowledgment is made to the Royal Commissioners for the Exhibition of 1851 for an Overseas Studentship (to R. B. J.) and to the New Zealand Government for a National Research Fellowship (to J. M.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, October 5th*, 1954.]

The Photodimerisation of Some Unsaturated Cyclic Sulphones.

By W. DAVIES and F. C. JAMES.

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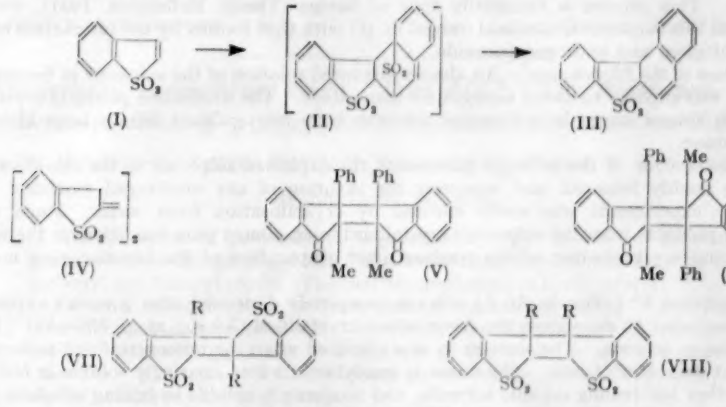
Thionaphthen 1 : 1-dioxide (I) in benzene solution is converted by sunlight into a stable dimer, m. p. 330—331°, which is considered to contain a central *cyclo*butane structure as in (VII) or (VIII). The sulphones of 3-bromo- and 3 : 4-dimethyl-thiophen similarly give high-melting crystalline dimers presumably of the same type, but intractable oils are formed from the three non-cyclic sulphones investigated containing the ·SO_2·CH:CH· group.

IT has been noted in this Department that crystalline thionaphthen 1 : 1-dioxide (I) undergoes a change when exposed to light. It is now found that in benzene solution the pure dioxide, m. p. 142°, is completely converted by long exposure to sunlight into a sparingly soluble crystalline dimer, m. p. 330—331°. The stability of this towards oxidising and reducing agents shows the absence of a double bond, and therefore structures of type (IV) are untenable. Though the monomer cannot be isolated when the dimer is heated, the latter in boiling butyl phthalate (b. p. 338—340°) slowly decomposes forming sulphur dioxide and fluorescent 10 : 11-dihydro-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (III). The precursor of this is considered to be the dimer (II), which is accepted (Bordwell, McKellin, and Babcock, *J. Amer. Chem. Soc.*, 1951, **73**, 5566; Davies, Gamble, and Savige, *J.*, 1952, 4678) as the unisolated intermediate adduct in the conversion of (I) into (III) by heat. The photodimer cannot be (II), which on steric grounds is inherently unstable,* and from analogy with related, though simpler, structures (Davies and James, *J.*, 1954, **16**; Bailey and Cummins, *J. Amer. Chem. Soc.*, 1954, **76**, 1938) would be expected to lose the sulphur bridge easily. The conversion of the photodimer into (III) is evidently due, at the boiling point of butyl phthalate, to dissociation of the photodimer into (I), which when heated readily gives (III).

Since no dimerisation of 2 : 3-dihydrothionaphthen 1 : 1-dioxide is brought about by illumination even for two months under the above conditions, the 2 : 3-double bond in (I) seems responsible for its self-addition. Polar molecules are known to add to this bond (Challenger and Clapham, *J.*, 1948, 1615; Bordwell and McKellin, *J. Amer. Chem. Soc.*, 1950, **72**, 1985), and it is also known that in some sulphur-free compounds electrophilic groups (usually CO and CO_2H) activate double bonds which are not only polarised but also take part in photodimerisation. The latter phenomenon has been reviewed by Mustafa (*Chem. Reviews*, 1952, **51**, 1), and perhaps the nearest formal analogy with (I) is 2-methyl-3-phenylindanone, the two photodimers of which are accepted as being the dimethyldiphenyltruxones (V) and (VI). Numerous photodimers from monomers containing the C:C·CO group are accepted as containing the *cyclo*butane ring, for which, however, the main chemical evidence is the absence of a double bond in the photodimers, and their easy dissociation by heat. But for the case of stilbamidine $[NH_2·C·(:NH)·C_6H_4·CH:]_2$, not mentioned by Mustafa, proof exists that its dimer contains the *cyclo*butane ring (Fulton and Dunitz, *Nature*, 1947, **160**, 161).

* We are indebted to a Referee for drawing this to our attention.

The rejection of the theoretically possible structures (II) and (IV), and analogy with the photodimers reviewed by Mustafa, makes it likely that the single photodimer obtained from (I) contains a *cyclo*butane ring. The photodimer would then be (VII) or (VIII), and it is unfortunate that attempts to obtain direct experimental evidence for either structure have failed. Fission with alkaline reagents cannot be effected, and desulphurisation with Raney nickel in boiling ethanol to produce ethylbenzene is ambiguous. A diphenyl*cyclo*butane was expected, and though this is apparently not known to suffer hydrogenolysis, it may nevertheless have done so even more thoroughly than does ethyl*cyclo*butane under more drastic conditions in the presence of platinised carbon (Kazanskii and Yu. Lukina, *Doklady Akad. Nauk U.S.S.R.*, 1950, **74**, 263; *Chem. Abs.*, 1951, **45**, 2879), or alternatively the dimer (despite the relatively low temperature) may have dedimerised to yield (I) which is desulphurised to give ethylbenzene.



3-Bromothionaphthen 1 : 1-dioxide was photodimerised in order to ascertain whether angular (VII; R = Br) or linear (as VIII; R = Br) dimerisation was favoured. Since the bromine atom in 3-bromo-2 : 3-dihydrothionaphthen 1 : 1-dioxide is very reactive, sodium iodide could be expected to react with the photodimer if it were (VIII; R = Br) to cause complete loss of halogen with the formation of a double bond (cf. Finkelstein, *Ber.*, 1910, **43**, 1530), behaviour which would not take place with the isomer (VII; R = Br). However, sodium iodide does not react with the photodimer, of which the successful debromination by zinc and acetic acid does not indicate the structure. Both this dimer and that of (I) are non-fluorescent and are stable to heat and oxidising agents.

3 : 4-Dimethylthiophen 1 : 1-dioxide also gives a high-melting crystalline photodimer, the stability of which to permanganate at room temperatures indicates that it contains no exocyclic methylene group. Moreover, the behaviour of the compound at its melting point recalls that of a number of substances shortly to be described, which contain the $\cdot SO_2 \cdot C{:}C$ group in a ring. The structure of this photodimer is being further studied in connection with that of the monomer and related monomers, about which there is confusion in the literature (Bailey and Cummins, *J. Amer. Chem. Soc.*, 1954, **76**, 1933).

Though in the only cases investigated photodimerisation occurs smoothly when the $\cdot SO_2 \cdot CH{:}CH \cdot$ is in a ring, intractable oils are obtained after the irradiation by moderate sunlight for three weeks of benzene solutions of phenyl vinyl sulphone, styryl *p*-tolyl sulphone, and 3-bromo-1-phenylsulphonylprop-1-ene (Culvenor, Davies, and Savige, *J.*, 1949, 2205).

Experimental

Preparation of the Sulphones.—Thionaphthen, oxidised as described by Davies, Gamble, and Savige (*J.*, 1952, 4679) except that the oxidising mixture was heated on the water-bath for 1 hr. instead of over a flame, again gave the same yields of 9-thia-3 : 4-benzofluorene 9 : 9-

dioxide, m. p. 233—234°, and thionaphthen 1 : 1-dioxide, m. p. 142°. 3-Bromothionaphthen (Komppa, *J. prakt. Chem.*, 1929, **122**, 1319) was similarly converted into 3-bromothionaphthen 1 : 1-dioxide, m. p. 183·5—184° (Bordwell and Albisetti, *J. Amer. Chem. Soc.*, 1948, **70**, 1559). 2 : 3-Dihydrothionaphthen 1 : 1-dioxide, and its 3-bromo-derivative (made by the action of hydrogen bromide on thionaphthen 1 : 1-dioxide) were prepared as described by Bordwell and McKellin (*loc. cit.*). 3-Bromo-2 : 3-dihydrothionaphthen 1 : 1-dioxide is not only readily dehydrobrominated to regenerate the parent thionaphthen 1 : 1-dioxide when refluxed for 1 hr. with pyridine in benzene, but also when refluxed with sodium iodide in acetone, the solution, diluted with water, being then kept for a week at room temperature.

3 : 4-Dibromo-3 : 4-dimethylthiophen 1 : 1-dioxide (van Zuydewijn, *Rec. Trav. chim.*, 1938, **57**, 445) (2 g.) and pyridine (5 ml.) in benzene (20 ml.) were refluxed for 2 hr., then filtered from pyridine hydrobromide. The residual 3 : 4-dimethylthiophen 1 : 1-dioxide from the filtrate crystallised from water (yield, 0·8 g. of needles or plates, m. p. 120°), and then from ethanol (m. p. 120·5—121°) (Found : C, 50·2; H, 5·5; S, 21·9. Calc. for $C_6H_8O_2S$: C, 50·0; H, 5·6; S, 22·2%). This process is essentially that of Savige (Thesis, Melbourne, 1951), who also showed that this sulphone is identical (mixed m. p.) with that formed by the interaction of 3 : 4-dimethylthiophen and hydrogen peroxide.

Formation of the Photodimers.—An almost saturated solution of the sulphone in benzene in a silica flask was exposed to direct sunlight for many days. The irradiation products crystallised and though almost insoluble in common solvents, were recrystallised from a large amount of boiling acetone.

The dimerisation of the strongly fluorescent thionaphthen sulphone to the non-fluorescent dimer was readily followed, and moreover the isolation of any unchanged monomer in the preliminary experiments was easily effected by crystallisation from water. Much of the irradiation products from the sulphones crystallised in an almost pure condition on the walls of the flask, and crystallisation of the residues after evaporation of the benzene gave no other dimers.

Thionaphthen 1 : 1-dioxide (10 g.) was not completely dimerised after a week's exposure to sunlight, but after 20 days gave the *dimer* which crystallised (5·0 g.; m. p. 330—331°) from a large volume of acetone. The same m. p. was obtained when the unrecrystallised material was sublimed at 260—270°/1 mm. The dimer is insoluble in water, sparingly soluble in hot acetic acid and other low-boiling organic solvents, and moderately soluble in boiling ethylene glycol, from which it separates in small needles [Found : C, 57·7; H, 3·7; S, 19·5%; *M* (cryoscopic in *p*-bromophenol), 335, 353. $(C_8H_6O_2S_2)_2$ requires C, 57·9; H, 3·6; S, 19·3%; *M*, 332].

The dimer was unaffected by potassium permanganate in boiling acetone for 8 hr., by hydrogen peroxide in hot glacial acetic acid, or by lithium aluminium hydride in tetrahydrofuran. No fission occurred on 20 hours' refluxing in ethanolic sodium hydroxide, or in the use of sodamide and piperidine (Bradley, *J.*, 1938, 458) or sodium amalgam (Dably, Kenyon, and Mason, *J.*, 1952, 4881). The dimer dissolved unchanged in hot concentrated nitric acid, but was converted by hot mixed concentrated sulphuric and fuming nitric acids into an insoluble nitrogenous compound which could not be purified. The dimer slowly dissolved in boiling butyl phthalate, sulphur dioxide was evolved, and after 3 hours' refluxing the solution on cooling deposited crystals of 10 : 11-dihydro-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (III), m. p. and mixed m. p. with an authentic specimen, 181—182° (cf. Davies, Gamble, and Savige, *loc. cit.*).

Conversion of the Thionaphthen Sulphone Dimer into Ethylbenzene.—A suspension of the dimer (1·0 g.), Raney nickel (30 g.; prepared as described by Mozingo, Wolf, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1943, **65**, 1013) in ethanol (100 c.c.) and acetone (100 c.c.) was refluxed for 5 hr., then diluted with water (500 c.c.), and distilled until the ethanol was removed. This distillate was again diluted with water (500 c.c.), and the ethanolic azeotrope formed two layers when diluted with water (200 c.c.). The upper layer, when dried ($CaCl_2$) and evaporated, yielded ethylbenzene (0·1 g.; b. p. 133—135°), oxidised by potassium permanganate to benzoic acid (m. p. and mixed m. p. 120—121°).

3-Bromothionaphthen 1 : 1-dioxide (3·0 g.), exposed to sunlight for 30 days, gave a sparingly soluble *dimer* which was recrystallised (1·2 g.; m. p. 314—315°) from acetone or more conveniently from ethylene glycol (needles) [Found : C, 38·9; H, 2·1; S, 13·5%; *M*, 470, 452. $(C_8H_5O_2SBr)_2$ requires C, 39·2; H, 2·0; S, 13·1%; *M*, 490]. It was recovered unchanged after refluxing with sodium iodide in acetone and in acetonylacetone. When refluxed with zinc dust and acetic acid for 3 hr. it gave a bromine-free product (in amount too small for analysis) which crystallised from ethylene glycol in non-fluorescent rods, m. p. >360°, which slowly became light buff after exposure to air.

Irradiation of 3 : 4-dimethylthiophen 1 : 1-dioxide (1·0 g.) in sunlight for 28 days yielded the non-fluorescent *dimer* (0·6 g.), m. p. 290—291° (decomp.) [Found : C, 50·1; H, 5·5; S, 22·2%; *M*, 295, 310. $(C_6H_8O_2S)_2$ requires C, 50·0; H, 5·6; S, 22·2%; *M*, 288]. It crystallises from acetone and *cyclo*hexanone in compact prisms of high refractive and dispersive power. At the m. p., which varies somewhat with the rate of heating, there is sudden evolution of sulphur dioxide, and a xylene solution of the yellowish-brown residue had a weak yellow fluorescence. The dimer is appreciably soluble in cold water, and neither this solution nor one in acetone decolorised dilute potassium permanganate solutions in 5 min. at room temperature.

The three crystalline photodimers obtained in this work are too insoluble in camphor for their molecular weights to be obtained by the Rast process. *p*-Bromophenol has been used instead (by F. C. J.).

The authors are indebted to the Dunlop Rubber Company of Australia Ltd. for a research scholarship (to F. C. J.), and to Drs. W. E. Savige and Q. N. Porter for assistance. The microanalyses were carried out by Dr. W. Zimmermann and his staff.

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Quaternary Ammonium Salts. Part III. The Formation and Decomposition of* p-*Aroylphenylethyldimethylammonium Salts.*

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The formation of these salts (I) is governed by the $-M$ effect of the aroyl group, which is the combined effect of the electronic displacements due to the carbonyl and the aryl group. Thermal decomposition of the iodides (I; X = I) leads, with one exception, to formation of the corresponding *N*-ethyl-*N*-methylaminobenzophenones (B). However, decomposition with alcoholic sodium methoxide gives rise to a mixture of the base (B) and the methyl ether (A). The ratio of A to B depends on the nature and on the position of the substituent in the aryl group.

THIS work deals with the effect of the *p*-aroyl group on the formation and decomposition of quaternary ammonium salts (cf. Part I, Fahim and Galaby, *J.*, 1950, 3529; Part II *). *N*-*p*-Aroylphenyl-*N*-ethyl-*NN*-dimethylammonium ethyl sulphates (I; X = $EtSO_4$) were formed by heating the corresponding tertiary bases with ethyl sulphate at 115—130°. The quaternary salt was estimated as picrate or iodide. Formation of the quaternary salt is inhibited by increase of the $-M$ effect of the aroyl group, which is the combined effect of the electronic displacements due to the carbonyl and the aryl group. The relative ease of formation of the quaternary salt from 4-dimethylamino-4′-methylbenzophenone (II; R = Me) is due to the decrease in the $-M$ effect of the carbonyl group caused by the $+I$ and probably by the hyperconjugation effect of the methyl group.

(I) (II)

The results showed, however, that process (*a*) (see II) is retarded by electron-repelling substituents, and enhanced by electron-attracting ones in ring E. This explains the low tendency of certain bases to form quaternary ammonium salts, *e.g.*, *p*-dimethylaminobenzaldehyde (cf. Part I, *loc. cit.*) and 4-dimethylamino-4′-nitrobenzophenone.

The final decomposition of the quaternary iodides led [except with (I; Ar = *o*-bromophenyl, X = I), which gives the corresponding dimethylamino-base] to the corresponding *N*-ethyl-*N*-methylaminobenzophenone (B); a similar result was reported in Parts I and II (*locc. cit.*).

However, when the same quaternary ammonium iodides were decomposed by alcoholic sodium methoxide the same *N*-ethyl-*N*-methylaminobenzophenones (B) were obtained mixed

* Part II, *J.*, 1951, 2761.

with the corresponding methyl ethers (A). The ratio of A to B varied from one iodide to another, depending mainly on the nature and on the position of the substituent already

(A) *p*-Ar·CO·C_6H_4·OMe *p*-Ar·CO·C_6H_4·NMeEt (B)

present in the aryl group. This formation of two products suggests the presence of two positive centres (*a*) and (*b*) in the molecule (I), the ratio A : B being governed by the relative electron densities there. The formation of the ether (A) seems to proceed by the bimolecular nucleophilic substitution mechanism S_N2 (cf. Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 802). The increase in the ratio A : B in the order Ar = *p*- < *m*- < *o*-bromophenyl indicates that the bromine atom is probably operating by its $-I$ effect only.

This explains why the *m*-acetyl quaternary iodide gave only the tertiary base when decomposed by alkaline sodium methoxide, since the *m*-oriented acetyl group will impart a very weak positive charge on a carbon atom attached to nitrogen by its $-I$ effect, which is not sufficient for the nucleophilic attack by the methoxyl ion.

Experimental

The quaternary ammonium salts (ethosulphate, picrate, and iodide) were prepared as described in Part I (*loc. cit.*). The quaternary ammonium iodides were decomposed by heating them above the m. p. for some time. The resulting tertiary base was extracted with a suitable solvent (ether, alcohol, or toluene) and identified by analysis and by mixed m. p. with the starting tertiary base.

The decomposition with alkali was effected by refluxing the quaternary iodide (0·005 mole) with methyl-alcoholic sodium methoxide [from sodium (0·3 g.) and absolute methyl alcohol (20 ml.)] for 3 hr. Alcohol was then evaporated and the product was extracted with 5N-hydrochloric acid (30 ml.). The neutral product was the corresponding *p*-methoxybenzophenone. The acid solution was made alkaline, and the base liberated was identified by m. p. and mixed m. p. with the product obtained from the thermal decomposition. The recorded ratios of the neutral portion (A) to the base (B) are semiquantitative, since a blank experiment on the base showed that it could be recovered in 95% yield. The yields recorded were the mean of at least two concordant results. A higher concentration of sodium methoxide caused resinification in the case of the 4-*m*-nitrobenzoyl quaternary iodide.

4-Dimethylaminobenzophenone.—p-Benzoylphenylethyldimethylammonium picrate (95% yield from the ethosulphate; 5 hr. at 115—120°), crystallised from alcohol, had m. p. 175—176° (Found : C, 57·4; H, 4·7. $C_{23}H_{22}O_9N_4$ requires C, 57·3; H, 4·6%). The *iodide*, crystallised from methanol–ether, had m. p. 154° (decomp.) (Found : I, 33·3. $C_{17}H_{20}ONI$ requires I, 33·3%). On thermal decomposition, the iodide gave *4-ethylmethylaminobenzophenone*, colourless crystals (from ethanol), m. p. 77—78° (Found : C, 79·6; H, 7·1. $C_{16}H_{17}ON$ requires C, 80·3; H, 7·1%). The alkaline decomposition gave the same compound (B) (0·75 g.), m. p. 76°, and 4-methoxybenzophenone (A) (0·1 g.), m. p. 61° (Ullmann and Goldberg, *Ber.*, 1902, **35**, 2814, gave m. p. 61—62°). The molar ratio B : A was 1 : 0·15.

4-Dimethylamino-4′-methylbenzophenone.—Ethyldimethyl-p-toluoylphenylammonium picrate, obtained in 90% yield from the ethosulphate (3 hr. at 115—120°) and crystallised from ethanol, had m. p. 178—179° (Found : C, 57·9; H, 4·7. $C_{24}H_{24}O_9N_4$ requires C, 58·1; H, 4·8%). The *iodide*, crystallised from methanol–ether, had m. p. 135° (decomp.) (Found : I, 32·1. $C_{18}H_{22}ONI$ requires I, 32·2%). Thermal decomposition of the iodide gave *4-ethylmethylamino-4′-methylbenzophenone*, colourless crystals (from ethanol), m. p. 103—104° (Found : C, 80·0; H, 7·6. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·5%). The alkaline decomposition gave the same product (0·85 g.) and 4-methoxy-4′-methylbenzophenone (0·2 g.), m. p. 89° (Jones, *J.*, 1936, 1854, gave m. p. 90—91°). Molar ratio B : A = 1 : 0·26.

4-Dimethylamino-4′-methoxybenzophenone.—4-p-*Anisoylphenylethyldimethylammonium picrate* (88% from the ethosulphate; 6 hr. at 115—120°), crystallised from water, had m. p. 185° (Found : C, 56·4; H, 4·6. $C_{24}H_{24}O_{10}N_4$ requires C, 56·3; H, 4·7%); the *iodide*, crystallised from methanol–ether, had m. p. 137—138° (decomp.) (Found : I, 31·3. $C_{18}H_{22}O_2NI$ requires I, 30·9%). On thermal decomposition, the iodide gave *4-ethylmethylamino-4′-methoxybenzophenone*, colourless crystals (from ethanol), m. p. 107° (Found : C, 75·5; H, 7·2. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1%). The alkaline decomposition gave the same compound (0·7 g.), m. p. 106°, and 4 : 4′-dimethoxybenzophenone (0·18 g.), m. p. 144° (Unger, *Annalen*, 1933, **504**, 285, gave m. p. 146°). Molar ratio B : A = 1 : 0·28.

4-*Bromo*-4′-*dimethylaminobenzophenone*.—4-p-*Bromobenzoylphenylethyldimethylammonium picrate*, formed in 85% yield from the ethosulphate (10 hr. at 120—125°) and crystallised from ethanol, had m. p. 178° (Found: C, 49·2; H, 3·9. $C_{23}H_{21}O_8N_4Br$ requires C, 49·2; H, 3·7%). The colourless *iodide* (from methanol) had m. p. 160° (decomp.) (Found: I, 27·7. $C_{17}H_{19}ONBrI$ requires I, 27·6%). Thermal decomposition gave 4-*bromo*-4′-*ethylmethylaminobenzophenone*, m. p. 83—84° (from ethanol) (Found: C, 59·9; H, 5·0. $C_{16}H_{16}ONBr$ requires C, 60·4; H, 5·0%). The alkaline decomposition gave the same ketone (0·75 g.), m. p. 82°, and 4-bromo-4′-methoxybenzophenone (0·29 g.), m. p. 154° (Jones, *loc. cit.*, gave m. p. 154°). Molar ratio B : A = 1 : 0·43.

3-*Bromo*-4′-*dimethylaminobenzophenone*.—This *ketone*, prepared by a method similar to that of Shah, Deshpande, and Chaubal (*J.*, 1932, 642), had m. p. 97·5—98·5° (from ethanol) (Found: C, 59·5; H, 4·8; N, 4·75; Br, 25·8. $C_{15}H_{14}ONBr$ requires C, 59·2; H, 4·6; N, 4·6; Br, 26·3%). 4-m-*Bromobenzoylphenylethyldimethylammonium picrate*, obtained in 80% yield from the ethosulphate (10 hr. at 120—125°) and crystallised from ethanol, had m. p. 156—157° (Found: C, 49·8; H, 3·7. $C_{23}H_{21}O_8N_4Br$ requires C, 49·2; H, 3·7%). The *iodide*, crystallised from methanol, had m. p. 159° (decomp.) (Found: I, 27·2. $C_{17}H_{19}ONBrI$ requires I, 27·6%). Thermal decomposition gave 3-*bromo*-4′-*ethylmethylaminobenzophenone*, colourless crystals, m. p. 82—83° (Found: C, 60·3; H, 5·2. $C_{16}H_{16}ONBr$ requires C, 60·4; H, 5·0%), and alkaline decomposition gave the same product (0·66 g.), m. p. 82°, and 3-bromo-4′-methoxybenzophenone (0·33 g.), m. p. 80° (Jones, *loc. cit.*, gave m. p. 80°). Molar ratio B : A = 1 : 0·54.

2-*Bromo*-4′-*dimethylaminobenzophenone*.—Prepared like the 3′-bromo-isomer, and crystallised from methanol, this *ketone* had m. p. 85° (Found: 60·0; H, 4·9; N, 4·4%). 4-o-*Bromobenzoylphenylethyldimethylammonium picrate*, made from the ethosulphate in 96% yield (6 hr. at 120—125°) and crystallised from ethanol, had m. p. 168—169° (Found: C, 49·6; H, 3·7%), and the *iodide* had m. p. 154° (decomp.) (from methanol–ether) (Found: I, 26·9%). Thermal decomposition of the latter gave 2-bromo-4′-dimethylaminobenzophenone, m. p. 85°, and alkaline decomposition gave this ketone (0·35 g.), m. p. 83°, together with 2-bromo-4′-methoxybenzophenone (0·7 g.), m. p. 94° (Jones, *loc. cit.*, gave m. p. 96°). Molar ratio B : A = 1 : 2·18.

4-*Dimethylamino*-4′-*nitrobenzophenone*.—*Ethyldimethyl*-p-*nitrobenzoylphenylammonium picrate* (75% yield from the ethosulphate; 12—13 hours' heating at 125—130°), crystallised from acetone, had m. p. 201—202° (Found: C, 52·3; H, 4·0. $C_{23}H_{21}O_{10}N_5$ requires C, 52·4; H, 4·0%), and the *iodide* crystallised from methanol–ether in deep red crystals, m. p. 123° (decomp.) (Found: I, 29·4. $C_{17}H_{19}O_3N_2I$ requires I, 29·8%). The thermal decomposition product of the iodide was crystallised from toluene to give 4-*ethylmethylamino*-4′-*nitrobenzophenone* in deep orange-coloured plates, m. p. 168—170° (Found: 68·2; H, 5·5. $C_{16}H_{16}O_3N_2$ requires C, 67·6; H, 5·6%). The alkaline decomposition gave a mixture of two unidentified products.

4-*Dimethylamino*-3′-*nitrobenzophenone*.—*Ethyldimethyl*-m-*nitrobenzoylphenylammonium picrate* (83% yield from the ethosulphate; 7 hr. at 120—125°), crystallised from acetone–light petroleum (b. p. 50—60°), had m. p. 136—137° (Found: C, 52·4; H, 4·1. $C_{23}H_{21}O_{10}N_5$ requires C, 52·4; H, 4·0%). The *iodide* formed needles (from methanol–ether), m. p. 153° (decomp.) (Found: I, 29·4. $C_{17}H_{19}O_3N_2I$ requires I, 29·8%). On thermal decomposition it gave 4-*ethylmethylamino*-3′-*nitrobenzophenone*, yellow plates [from toluene–light petroleum (b. p. 50—60°)], m. p. 136—137° (Found: C, 68·2; H, 5·6%), and alkaline decomposition gave the same product (0·26 g.), m. p. 135°, and 4-methoxy-3′-nitrobenzophenone (0·23 g.), m. p. 91° (Jones, *loc. cit.*, gave m. p. 93°). Molar ratio B : A = 1 : 1.

3-*Acetyl*-NN-*dimethylaniline*.—This was obtained from methyl sulphate and a methyl-alcoholic solution of *m*-aminoacetophenone, b. p. 148°/13 mm. (Rupe, Braun, and von Zembruski, *Ber.*, 1901, **34**, 3522); its *picrate* crystallised from water in yellow needles, m. p. 139—141° (Found: C, 48·7; H, 4·1. $C_{16}H_{16}O_8N_4$ requires C, 49·0; H, 4·1%), and its *ethiodide* (from methanol–ether) had m. p. 175—178° (decomp.) (Found: I, 38·8. $C_{12}H_{18}ONI$ requires I, 39·8%). The quaternary *picrate* (from the iodide) formed yellow crystals, m. p. 125—126° (Found: C, 51·5; H, 4·7. $C_{18}H_{20}O_8N_4$ requires C, 51·4; H, 4·8%), from water. Thermal decomposition of the quaternary iodide gave 3-acetyl-*N*-ethyl-*N*-methylaniline; its *picrate*, crystallised from water, had m. p. 129—131° (Found: C, 50·2; H, 4·3. $C_{17}H_{16}O_8N_4$ requires C, 50·2; H, 4·4%). The alkaline decomposition of the same iodide gave only 3-acetyl-*N*-ethyl-*N*-methylaniline, the picrate of which was identical with that of the thermal decomposition product.

The iodine in the iodides was determined by boiling them with alcoholic silver nitrate.

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Studies in the Vitamin D Field. Part I. Synthesis of Trienes containing the Tachysterol Chromophore.

By E. A. Braude and O. H. Wheeler.

[Reprint Order No. 5729.]

*cyclo*Hexylidene- and 2′-methyl*cyclo*hexylidene-acetaldehyde have been prepared by a number of methods. Reaction of the aldehydes with *cyclo*hexenyl-lithium, followed by anionotropic rearrangement and dehydration, gave the trienes (IV*a* and *b*). These model experiments adumbrate a synthetical route to tachysterol derivatives.

The structures and light-absorption properties of tachysterol and calciferol are discussed.

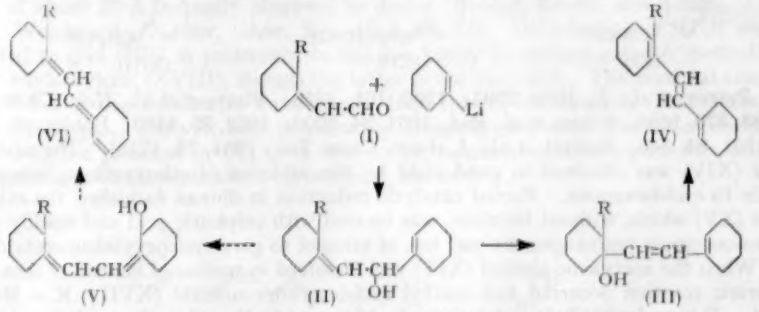
Although the chemistry of calciferol and its congeners was first elucidated some twenty years ago, the D group of vitamins is exceptional in that no synthesis of practical value of any of its members has yet been effected. In a formal sense, the total synthesis of calciferol has recently been achieved by way of methyl 3-oxo*ætio*cholatrienate and cholestanol (Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223) and by way of *ætioallo*bilianic acid and cholestanol (Cardwell, Cornforth, Duff, Holtermann, and Robinson, *J.*, 1953, **361**) but these schemes involve some 50 steps and their significance lies primarily in the methodology of steroid synthesis rather than in the vitamin D field. A few attempts aimed at a direct synthesis of calciferol have been recorded (Burkhardt *et al.*, *J.*, 1938, **545**, **987**; 1940, **10**; Milas and Alderson, *J. Amer. Chem. Soc.*, 1939, **61**, **2534**; Dimroth and Jonsson, *Ber.*, 1938, **71**, **1333**, **1346**, **2658**; Dimroth, *Ber.*, 1943, **76**, **634**; Raphael and Sondheimer, *J.*, 1950, 3185) but, compared with the enormous efforts expended on other similar problems, the extent of such investigations has been relatively limited. This problem merits further attention, not only in view of the great physiological importance of calciferol, but also because the synthetical difficulties presented by the tricyclic system appear, at least on paper, rather less formidable than those posed by the tetracyclic steroid skeleton. Furthermore, D vitamins are not only generated from steroids, but can also be transformed back into steroids with considerable ease (see Fieser and Fieser, "Chemistry of Natural Products Related to Phenanthrene," Reinhold Publ. Corpn., New York, 1949). In addition, there are still certain stereochemical and other features of vitamin D and its progenitors which have not been completely clarified.

The present series will describe some new approaches to the synthesis of vitamin D and related compounds. Although we are far from having achieved the final goal, an interim report is now submitted since the problem has recently been taken up in several other laboratories, particularly by Inhoffen and his co-workers who have effected a partial synthesis of an isomer of calciferol designated as *iso*tachysterol and of its methyl ether (*Chem. Ber.*, 1954, **87**, 1, 187; cf. Inhoffen and Brückner, *Fortschr. Chem. org. Naturstoffe*, 1954, **11**, 83).

This and the following paper deal with experiments in which new routes to simple analogues containing the chromophoric systems of calciferol and tachysterol, respectively, have been explored. Since tachysterol is believed to be the immediate precursor of calciferol in the photochemical preparation of the latter from ergosterol, methods leading to either of these two systems are equally of interest. In the present work, the tachysterol analogues (IV*a*, *b*) have been synthesised by the addition of *cyclo*hexenyl-lithium (Braude and Coles, *J.*, 1950, **2014**; Braude, Bruun, Weedon, and Woods, *J.*, 1952, **1414**) to *cyclo*hexylidene- and 2′-methyl*cyclo*hexylidene-acetaldehyde (I*a*, *b*), to give the diallylic alcohols (II*a*, *b*), followed by anionotropic rearrangement to the conjugated isomers (III*a*, *b*) and dehydration.

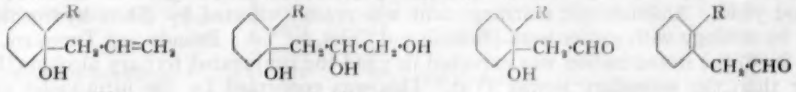
The aldehyde (I*b*) has not previously been described, but the parent compound (I*a*) has been prepared, though in low yield, by the ozonisation of 1-allyl*cyclo*hexanol (VII*a*) (Burkhardt *et al.*, *locc. cit.*) as well as from 1-ethynyl*cyclo*hexanol (Dimroth, *Ber.*, 1938, **71**,

1333; Chaco and Iyer, *Current Sci.*, 1953, **22**, 240). Attempts to improve the conversion of 1-allyl*cyclo*hexanol into the aldehyde met with little success; for example, hydroxylation with performic acid to give the triol (VIII*a*) followed by fission with periodic acid



(*a*, R = H; *b*, R = Me; throughout this paper.)

and dehydration of the resulting hydroxy-aldehyde (IX*a*) with iodine furnished even lower overall yields and the product was contaminated with the unconjugated isomer (X*a*). Fortunately, the direct conversion of 1-allyl-2-methyl*cyclo*hexanol (VII*b*), obtained from 2-methyl*cyclo*hexanone and allylmagnesium chloride, into 2′-methyl*cyclo*hexylideneacetaldehyde (I*b*) by ozonisation proceeds in considerably better yield (70%) than with the lower homologue (35%). The product was again contaminated with the unconjugated isomer (X*b*) as well as with the hydroxy-aldehyde (IX*b*) which could, however, be largely

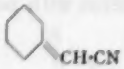


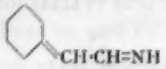
separated by careful fractionation. 2′-Methyl*cyclo*hexylideneacetaldehyde (I*b*), like its lower homologue (I*a*) (cf. Dimroth, *loc. cit.*), is rather unstable and even the best fractions showed an oxygen-content in excess of that calculated. The aldehyde was characterised by a semicarbazone and a 2 : 4-dinitrophenylhydrazone, the light absorption properties of which confirmed the absence of unconjugated components in the purified aldehyde.

Some possible alternative methods for the preparation of the aldehydes (I) were also investigated. The first envisaged the partial reduction of *cyclo*hexylideneacetonitrile (XI) which is readily accessible from *cyclo*hexylideneacetic acid (Kandiah and Linstead, *J.*, 1929, 2139; Cope *et al.*, *Org. Synth.*, 1951, **31**, 25), to the imine (XII), followed by hydrolysis. Partial reductions of this type have been successfully effected with several aliphatic nitriles by means of lithium aluminium hydride (Henne, Pelley, and Alm, *J. Amer. Chem. Soc.*, 1950, **72**, 3370; Yandik and Larsen, *ibid.*, 1951, **73**, 3534; Smith and Rogier, *ibid.*, p. 4048; Lowy, *ibid.*, 1952, **74**, 1354) as well as with aromatic nitriles (Braude and Gore, unpublished work). In the present case, however, reduction of the ethylenic bond occurred in preference to that of the cyano-group and *cyclo*hexylacetonitrile (XIII) was obtained, identified by hydrolysis to *cyclo*hexylacetic acid. Presumably, 1 : 4-addition to the C=C–C≡N system is involved, analogous to that which has been observed with ethylenic ketones (Lutz and Hinkley, *ibid.*, 1950, **72**, 4091; cf. Hochstein and Brown, *ibid.*, 1948, **70**, 3484), vinylacetylenes (Bharucha and Weedon, *J.*, 1953, 1584; Bates, Jones, and Whiting, *J.*, 1954, 1854), and other conjugated systems. 1 : 4-Reduction of conjugated ethylenic nitriles by lithium aluminium hydride appears to be the rule when a deficiency of hydride is employed; thus, 1-cyano*cyclo*hexene gave 1-cyano*cyclo*hexane. By contrast, *cyclo*hexenylacetonitrile in which the two unsaturated groups are not conjugated, is reduced to the ethylenic amine in good yield (Schnider and Hellerbach, *Helv. Chim. Acta*, 1950, **33**, 1437).

A second method, which is more successful, is based on 1-ethoxyethynyl*cyclo*hexanol

(XIV) and is analogous to that previously used for other ethylenic aldehydes (Arens and van Dorp, *Rec. Trav. chim.*, 1948, **67**, 973; 1951, **70**, 289; Heilbron, Jones, *et al.*, *J.*, 1949,


(XI)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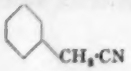
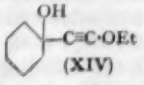
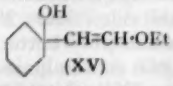
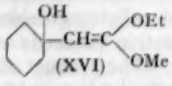
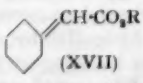

(XIII)

1823; Petrov *et al.*, *J.*, 1950, 2393; 1952, 161, 3358; Plattner *et al.*, *Helv. Chim. Acta*, 1950, **33**, 370, 1088; Schinz *et al.*, *ibid.*, 1951, **34**, 2009; 1952, **35**, 1469; Bohlmann, *Chem. Ber.*, 1951, **84**, 545; Sarrett *et al.*, *J. Amer. Chem. Soc.*, 1954, **76**, 1715). The acetylenic alcohol (XIV) was obtained in good yield by the addition of ethoxyethynylmagnesium bromide to *cyclo*hexanone. Partial catalytic reduction in dioxan furnished the ethylenic alcohol (XV) which, without isolation, was treated with sulphuric acid and readily underwent anionotropic rearrangement and loss of ethanol to give *cyclo*hexylideneacetaldehyde (I*a*). When the acetylenic alcohol (XIV) was dissolved in methanol instead of dioxan, an exothermic reaction occurred and methyl *cyclo*hexylideneacetate (XVII; R = Me) was formed. This undoubtedly involves initial addition of methanol to the triple bond to give (XVI), followed by (allylic) rearrangement and elimination of ethanol; direct (propargylic) rearrangement of (XIV) to the ethyl ester (XVII; R = Et) takes place only under quite strongly acid conditions (cf. Braude, *Quart. Reviews*, 1950, **4**, 404).


(XIV)


(XV)

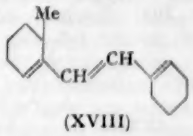

(XVI)


(XVII)

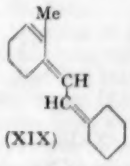
Addition of *cyclo*hexenyl-lithium to *cyclo*hexylideneacetaldehyde gave the alcohol (II*a*) in good yield. Anionotropic rearrangement was readily effected by dilute hydrochloric acid; by analogy with earlier work (Braude and Coles, *loc. cit.*; Braude and Timmons, *J.*, 1950, 2006) the isomerisation was expected to yield the conjugated tertiary alcohol (III*a*) rather than the secondary isomer (V*a*). This was confirmed by the ultra-violet light absorption properties ($\lambda_{max.}$ 2360 Å, ε 18,000) which correspond to those of tri- rather than of a tetra-alkylated diene and by the formation of a well-crystallised adduct with maleic anhydride; the diene system in (V*a*) would be sterically prevented from undergoing a Diels–Alder reaction. Dehydration of the alcohol by distillation from potassium hydrogen sulphate afforded 1 : 2-di*cyclo*hexenylethylene (IV*a*) as a liquid showing characteristic triple-peak absorption in the 2700-Å region (see Table). Like other hydrocarbons of this type (for references, see p. 320) and like tachysterol itself (Grundmann, *Z. physiol. Chem.*, 1938, **252**, 151), the triene (IV*a*) avidly absorbs oxygen and was not obtained analytically pure, but its light-absorption properties are in good agreement, when allowance is made for the oxygen content, with those recorded by Burkhardt and Hindley (*J.*, 1938, 987). These workers prepared the triene by the pyrolysis of 1 : 2-di-1′-acetoxy*cyclo*hexylethylene, which they obtained in turn by partial catalytic hydrogenation and acetylation of di-1′-hydroxy*cyclo*hexylacetylene. This method might be expected to lead to a triene with *cis*-configuration at the central double bond, but it must be presumed that inversion took place during pyrolysis since the high intensity of the ultra-violet absorption indicates a *trans*-configuration (Koch, *Chem. and Ind.*, 1942, **61**, 273; cf. Braude and Waight, "Progress in Stereochemistry," Vol. 1, Chapter 4, Butterworths, London, 1954). The *trans*-configuration is also to be expected for the product obtained in the present work, since anionotropic rearrangement is known to lead normally to the less sterically hindered arrangement at the new double bond (Braude and Coles, *J.*, 1951, 2085).

Addition of *cyclo*hexenyl-lithium to 2′-methyl*cyclo*hexylideneacetaldehyde and the rearrangement of the alcohol (II*b*) proceeded readily and in a similar manner. In contrast to the lower homologue (III*a*), however, the isomerisation product (III*b*) did not form a Diels–Alder adduct with maleic anhydride. Dehydration of the alcohol (III*b*) furnished a triene which again could not be obtained free from oxygen-containing material. The ultra-violet absorption of the triene component (main maximum at 2710 Å, ε 40,000; see Table) was somewhat less well resolved, but otherwise closely resembled that of the lower

homologue (IV*a*) (main maximum at 2690 Å, ε 42,600) and the triene is assigned the structure (IV*b*). The small bathochromic displacement of 20 Å due to the additional methyl substituent in (IV*b*) is not unusual for triene systems (see Table) in contrast to the shifts of about 50 Å normally observed in dienes (Booker, Evans, and Gillam, *J.*, 1940, 1453; Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 72). Dehydration of (III*b*) would be expected to give (IV*b*) in preference to the less highly hyperconjugated 6′-methyldi*cyclo*hex-1′-enylethylene (XVIII), though the latter is not excluded. The maximal absorption of (IV*b*) lies at slightly shorter wave-lengths than that of the similarly (penta)substituted triene (XIX) ($\lambda_{max.}$ 2820 Å) first prepared by Dimroth (*loc. cit.*); the difference may be ascribed to the presence in (XIX) of two double bonds in exocyclic positions, known to have a small bathochromic effect (Woodward, *loc. cit.*).



(XVIII)



(XIX)

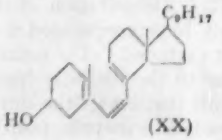
Ultra-violet light absorption of conjugated trienes.

	$\lambda_{max.}$ (Å)	$10^{-3}\varepsilon$
Hexatriene [1]	2475	68
	2575	79
	2675	56
2-Methylhexatriene [2]	2480	>21
	2570	>28
	2670	>22
2 : 5-Dimethylhexatriene [2]	2510	37
	2610	46
	2710	34
2-Methylhepta-1 : 3 : 5-triene [3]	2510	>29
	2610	>41
	2710	>31
1-*cyclo*Hexenylbutadiene [4]	2550	32
	2650	43
	2750	34
(IV*a*) [5, 6]	2595	35
	2690	42
	2810	37
(IV*b*) [6]	2710	34
	2810	34
(XIX) [6]	2820	20
Tachysterol [7]	2640	18
	2800	23
	2940	20
"*iso*Tachysterol" [8]	2800	31
	2900	41
	3020	31

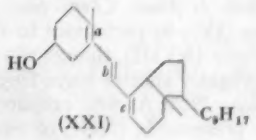
[1] Woods and Schwartzman, *J. Amer. Chem. Soc.*, 1948, **70**, 3394 (in *cyclo*hexane). [2] Braude and Timmons, *J.*, 1950, 2006 (in EtOH). [3] Kharasch, Nudenberg, and Sternfeld, *J. Amer. Chem. Soc.*, 1940, **62**, 2034 (solvent not stated). [4] Bates, Jones, and Whiting, *J.*, 1954, 1854. [5] Burkhardt and Hindley, *J.*, 1938, 987 (in EtOH). [6] Present work (in EtOH); cf. Dimroth, *Ber.*, 1938, **71**, 1333. [7] Windaus, Werder, and Lüttringhaus, *Annalen*, 1932, **499**, 188 (in C_6H_6). [8] Inhoffen, Brückner, and Gründel, *Chem. Ber.*, 1954, **87**, 1 (in Et_2O).

The method employed here for the preparation of the triene (IV*b*) adumbrates a synthetical route to tachysterol derivatives, provided analogous reactions can be carried out with 5′-hydroxy-2′-methyl*cyclo*hexylideneacetaldehyde and the appropriate ring CD components. Tachysterol has generally been formulated as containing a *cis*-ethylenic bond (XX), but most of the degradative evidence (Windaus, Werder, and Lüttringhaus, *Annalen*, 1932, **499**, 188; Grundmann, *loc. cit.*; von Werder, *Z. physiol. Chem.*, 1939, **260**, 119) is equally compatible with a *cis*- or a *trans*-structure (XXI). Actually there are two items of evidence which strongly favour a *trans*-configuration; first, the ready Diels–Alder reaction with citraconic anhydride, which is characteristic of tachysterol, and, secondly, the reported conversion of calciferol into tachysterol (Meunier and Thibaudet, *Compt. rend.*, 1946, **223**, 173; cf. Velluz, Petit, and Amiard, *Bull. Soc. chim.*, 1948, 1115) by successive iodination and de-iodination under conditions unlikely to lead to a *cis*-bond. Against these must be considered the relatively low intensity of the triene absorption reported for tachysterol ($\lambda_{max.}$ 2640 Å, ε 18,000; $\lambda_{max.}$ 2800, ε 23,000, $\lambda_{infl.}$ 2940 Å, ε 20,000; Windaus *et al.*, *loc. cit.*) which has, in fact, been adduced in support of the *cis*-configuration (Koch, *loc. cit.*). The spectral data were, however, obtained with a non-crystalline

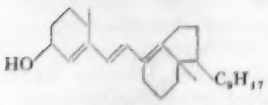
material for which no analytical figures were given, and in view of the exceptional ease of oxidation of tachysterol the low intensity might be due to the presence of less-absorbing products; as it happens, the ε value is almost identical with that obtained here for the partly oxidised triene (IV*b*) (see p. 323).



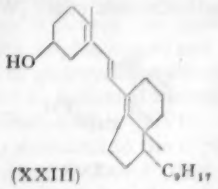
(XX)



(XXI)



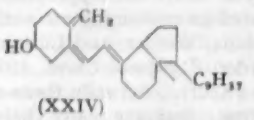
(XXII)



(XXIII)

Nevertheless, structure (XXI) also seems unsatisfactory, for two reasons. First, it has recently been shown by Stork, Wagle, and Mukherji (*J. Amer. Chem. Soc.*, 1953, **75**, 3197) that the diene system in 1-methyl-2-vinyl*cyclo*hexene, unlike that in 1-vinyl*cyclo*hexene, is unreactive towards maleic anhydride. If the analogy with 1-methyl-2-vinyl*cyclo*hexene is sound, the diene system *ab* in (XXI) should be unreactive in Diels–Alder addition, and certainly less reactive than the diene system *bc*, contrary to fact. Secondly, structure (XXI) does not explain the small, but definite, bathochromic shift of the maxima of tachysterol with respect to those shown by the synthetic trienes (IV*a*) and (IV*b*). (The long-wave-length inflection of 2940 Å recorded for tachysterol *in benzene* is very faint and part of the bathochromic shift may be apparent rather than real, arising simply from a change in the relative heights of the subsidiary peaks which undoubtedly represent partly resolved vibrational structure of the same electronic band.) All the facts appear, however, to be accommodated by structure (XXII) which contains a diene system analogous to that of 6-methyl-1-vinyl*cyclo*hexene, known to be highly reactive towards dienophiles (Stork *et al.*, *loc. cit.*), and a double bond in a bridgehead position, known to produce a small bathochromic shift. Structure (XXII) is also acceptable in relation to that (XXIII) assigned by Inhoffen *et al.* (*loc. cit.*) to "*iso*tachysterol" ($\lambda_{max.}$ 2900 Å), the further bathochromic shift being ascribed to the movement of the double bond in ring A to the more highly alkylated (and hyperconjugated) position.

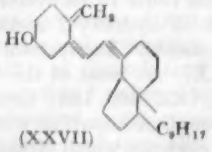
The considerable difference in the wave-lengths of the characteristic absorption of tachysterol-type and calciferol-type systems also deserves brief comment. Inhoffen *et al.* (*loc. cit.*) have ascribed this to "strong steric hindrance" in the latter. The *X*-ray diffraction work of Crowfoot and Dunitz (*Nature*, 1948, **162**, 608) makes it probable, how-



(XXIV)

(XXV)

(XXVI)



(XXVII)

ever, that calciferol exists in the extended *s-trans*-configuration (XXIV) rather than in the *s-cis*-configuration, and comparison with simpler systems (cf. Braude and Waight, *loc. cit.*, and references there cited) suggests that the deviation of the triene chromophore in (XXIV) from uniplanarity, though sufficient to decrease ε, would not result in a marked hypsochromic shift. The location of the maximum of calciferol at shorter wave-length ($\lambda_{max.}$ 2650 Å, ε 18,000) may be explained, however, at least in part, by the presence of a *cisoid* diene grouping and the consequent reduction in chromophore length (cf. Braude and Waight, *loc. cit.*); a similar, though, as would be expected, smaller displacement is found in

comparing the *cisoid* diene (XXV) ($\lambda_{max.}$ 2200 Å; Bailey and Golden, *J. Amer. Chem. Soc.*, 1953, **75**, 4780) and the *transoid* diene (XXVI) ($\lambda_{max.}$ 2300 Å; Gillam *et al.*, *loc. cit.*). The calciferol isomer " precalciferol " discovered by Velluz, Amiard, and Petit (*Bull. Soc. chim.*, 1948, 1115; 1949, 501), which is reported to show absorption of identical wavelength location with, but lower absorption intensity ($\lambda_{max.}$ 2650 Å, ε 9000) than, calciferol, may be the less stable stereoisomer (XXVII); the lower ε can be ascribed to steric hindrance between the hydrogen atoms attached to $C_{(6)}$ and $C_{(15)}$.

Experimental

Analytical data were determined in the microanalytical (Mr. F. H. Oliver and staff) and spectrographic (Mrs. I. A. Boston) laboratories of this Department. Oxygen determinations were carried out by Unterzaucher's method (*Ber.*, 1940, **73**, 391).

cyclo*Hexylideneacetaldehyde* (Ia).—*First method* (cf. Aldersley *et al.*, *J.*, 1940, 10). *cyclo*Hexanone (100 g.) and allyl chloride (80 g.) in ether (500 ml.) were added during 3 hr. to finely divided magnesium (24 g.) and iodine (0·1 g.) in ether, with rapid stirring and external cooling so as to maintain gentle refluxing. After a further hour, excess of ice-cold 2N-sulphuric acid was added, the ether layer was separated, and the aqueous layer extracted with ether. The combined ethereal solutions were washed with sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and fractionated, giving some unchanged *cyclo*hexanone and 1-allyl*cyclo*hexanol (69·5 g., 49%), b. p. 62—64°/3 mm., n_D^{24} 1·4730.

1-Allyl*cyclo*hexanol (50 g.) in acetic acid (50 ml.) was treated with ozone at 0° until absorption ceased (15 hr.). After addition of zinc dust (5 g.), the mixture was heated on the steam-bath for 20 min. and then poured into water (100 ml.) and extracted with ether. The ethereal solution was washed with sodium carbonate solution and water until nearly neutral, dried (Na_2SO_4), and fractionated, giving two main products. The first (b. p. 90°/10 mm.) was *cyclo*hexylideneacetaldehyde (14 g., 32%), n_D^{20} 1·5005, $\lambda_{max.}$ 2310 Å, ε 15,000 in hexane. It was characterised by the semicarbazone, m. p. 207—208° (from ethanol), $\lambda_{max.}$ 2740 Å, ε 28,000 in EtOH (Aldersley *et al.*, *loc. cit.*, give m. p. 205°, $\lambda_{max.}$ 2720 Å, ε 28,000; Dimroth, *Ber.*, 1938, **71**, 1333, gives m. p. 210°, $\lambda_{max.}$ 2720 Å, ε 32,000), and by the 2 : 4-*dinitrophenylhydrazone*, which was chromatographed on alumina in benzene and after crystallisation from ethyl acetate had m. p. 200°, $\lambda_{max.}$ 3870 Å, ε 27,400 in $CHCl_3$ (Found : C, 55·5; H, 5·5; N, 18·2. $C_{14}H_{16}O_4N_4$ requires C, 55·3; H, 5·3; N, 18·4%). The second product was 1-*hydroxy*cyclo*hexylacetaldehyde* (5 g., 18%), a viscous oil, b. p. 100°/0·5 mm., n_D^{20} 1·4828 (Found : C, 67·1; H, 10·1. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9%). It was characterised by a *semicarbazone*, prepared in, and crystallised from, aqueous solution, and having m. p. 165° (Found : N, 21·3. $C_9H_{17}O_2N_3$ requires N, 21·1%).

When the decomposition of the ozonide was conducted by addition of the acetic acid solution to boiling water (100 ml.) and zinc dust (4 g.), instead of as above, mainly the hydroxy-aldehyde was obtained.

Second method. 1-Allyl*cyclo*hexanol (14 g.) was added to formic acid (98%; 60 ml.) and hydrogen peroxide (30%; 12 ml.), the temperature being kept at 25—30° by external cooling. After being kept overnight at room temperature, the solution was concentrated under reduced pressure and the residue was treated with sodium hydroxide (8 g.) in water (20 ml.) for 15 min. at 50°. The resulting solution was saturated with sodium chloride and extracted with chloroform (6 × 50 ml.). After drying (Na_2SO_4), the chloroform was evaporated and the residue was distilled at 100° (bath-temp.)/10^{-3} mm., giving 1-(2 : 3-*dihydroxypropyl*)cyclo*hexanol* as a viscous oil (11·3 g.), n_D^{20} 1·4980, which solidified on being kept and crystallised from ethyl acetate in plates, m. p. 72° (Found : C, 62·2; H, 10·4. $C_9H_{18}O_3$ requires C, 62·0; H, 10·4%). Distillation at a higher temperature, or from a trace of potassium hydrogen sulphate resulted in dehydration to 1-(2 : 3-*dihydroxypropyl*)cyclo*hexene*, a viscous oil, b. p. 120° (bath-temp.)/10^{-3} mm., n_D^{23} 1·4900 (Found : C, 69·3; H, 10·5. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%).

1-(2 : 3-Dihydroxypropyl)*cyclo*hexanol (10 g.) in 50% aqueous methanol (40 ml.) was treated with periodic acid (10 g.) in water (10 ml.). The temperature rose to *ca.* 50°. After 10 min., water was added and the solution was extracted with chloroform. The extract was washed with water and aqueous sodium carbonate, dried (Na_2SO_4), and distilled, giving 1-hydroxy*cyclo*hexylacetaldehyde (4·5 g., 55%), b. p. 88—90°/0·1 mm. This was dehydrated by distillation from iodine (50 mg.), giving *cyclo*hexylideneacetaldehyde (2·1 g.), b. p. 93°/12 mm., n_D^{21} 1·4920, $\lambda_{max.}$ 2320 Å, ε 11,000 (in hexane), which contained some of the unconjugated isomer, 1-*cyclo*hexenylacetaldehyde, but formed a 2 : 4-dinitrophenylhydrazone, m. p. 202°, undepressed on admixture with the specimen described above.

Similar oxidation of 1-(2 : 3-dihydroxypropyl)*cyclo*hexene (1·7 g.) with periodic acid (2·1 g.) gave 1-*cyclo*hexenylacetaldehyde (1·1 g.), b. p. 100°/24 mm., n_D^{22} 1·4788, ε <500 at 2300 Å.

Treatment of 1-allyl*cyclo*hexanol (7·0 g.) in benzene (70 ml.) with lead tetra-acetate (22 g.) resulted in an unexpected rise in temperature (to 40°), and lead dioxide was precipitated. The solution was heated at 60° for ½ hr. and then cooled, washed with water and aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and distilled, giving *cyclo*hexanone (4·0 g., 80%), b. p. 48—50°/20 mm., identified by the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 158°.

Third method. Ethoxyacetylene was prepared by the following method adapted from Eglington, Jones, Shaw, and Whiting (*J.*, 1954, 1860).* Diethylchloroacetal (48 g.), prepared in 75% yield from vinyl acetate by Filachione's method (*J. Amer. Chem. Soc.*, 1939, **61**, 1705), was added during 1 hr. to a stirred solution of sodamide (from Na, 24 g.) in liquid ammonia (1 l.). The ammonia was allowed to evaporate under oxygen-free nitrogen, the last traces being cautiously removed at 50° (water-bath). Sodium chloride (65 g.) in water (200 ml.) was then added carefully to the solution at −40° and the ethoxyacetylene liberated was distilled off into a trap at −10°. The crude product (14·5 g., 66%) was washed with water and saturated aqueous sodium dihydrogen phosphate, dried (Na_2SO_4), and used without further purification.

Ethoxyacetylene (8 g.) in ether (30 ml.) was added at 0° to ethylmagnesium bromide (from Mg, 2·8 g., and ethyl bromide, 12·7 g.) in ether (70 ml.) and benzene (50 ml.). The solution was stirred for ½ hr. at 0° and then heated under reflux for ½ hr. *cyclo*Hexanone (12 g.) in ether (30 ml.) was added at 0°, and the mixture stirred for ½ hr. at room temperature and then under reflux for 1 hr. Excess of saturated aqueous ammonium chloride was added next at 0°, and the product worked up in the usual manner. Distillation of the ethereal solution gave 1-2′-*ethoxyethynyl*cyclo*hexanol* (13·4 g., 67%), b. p. 63—64°/0·1 mm., n_D^{21} 1·4820 (Found : C, 70·85; H, 9·75. $C_{10}H_{14}O_2$ requires C, 71·4; H, 9·6%). Omission of the benzene, or of either period of refluxing, led to much reduced yields. A poor yield was also obtained on reaction of sodioethoxyacetylene (prepared *in situ*) and *cyclo*hexanone in liquid ammonia.

1-2′-Ethoxyethynyl*cyclo*hexanol (10 g.) in dioxan (100 ml.) was hydrogenated in the presence of a palladium catalyst (1 g. ; Isler *et al.*, *Helv. Chim. Acta*, 1947, **30**, 1911 ; Lindlar, *ibid.*, 1952, **35**, 446), 1120 ml. (0·80 mol.) of hydrogen being absorbed during 10 hr. Sulphuric acid (2·5 ml.) was carefully added and the solution kept under nitrogen for 3 hr. at room temperature. Ice was then added and the product isolated with ether, giving *cyclo*hexylideneacetaldehyde (3 g.), b. p. 92°/12 mm., identified by the 2 : 4-dinitrophenylhydrazone (isolated in 90% yield), m. p. 202°, undepressed on admixture with the specimen described above. This derivative was also obtained on treating the solution of the hydrogenation product directly with Brady's reagent.

Use of a 0·3% palladium–calcium carbonate catalyst resulted in excessively slow and incomplete hydrogenation, while a similar 3% catalyst gave unselective reduction. Also, an attempted isolation of the vinyl ether gave a highly unstable product, b. p. 60—62°/0·3 mm., which rapidly darkened and polymerised on exposure to air, and afforded only a low yield of aldehyde on acid treatment.

Dissolution of 1-2′-ethoxyethynyl*cyclo*hexanol (3·7 g.) in methanol (35 ml.) gave, exothermally, *methyl* cyclo*hexylideneacetate* (3·2 g.), b. p. 50°/0·2 mm., n_D^{20} 1·4805, $\lambda_{max.}$ 2220 Å, ε 14,000 in EtOH (Found : C, 70·4; H, 9·4. $C_9H_{14}O_2$ requires C, 70·1; H, 9·2%). Shaking the *cyclo*hexanol (2·5 g.) with 5% aqueous sulphuric acid (25 ml.) for 1 hr. under nitrogen converted it into ethyl *cyclo*hexylideneacetate (1·9 g.) which was isolated with ether and had b. p. 104—106°/10 mm., n_D^{25} 1·4765, $\lambda_{max.}$ 2200 Å, ε 13,500 in EtOH (Kon and Linstead, *J.*, 1929, 1269, give b. p. 115°/14 mm., n_D^{18} 1·4799). The ester was hydrolysed by refluxing 10% aqueous sulphuric acid for 3 hr. under nitrogen, to the acid, m. p. and mixed m. p. 90°.

Reduction of cyclo*Hexylideneacetonitrile.*—α-Cyano-α-*cyclo*hexylideneacetic acid (m. p. 109°, $\lambda_{max.}$ 2340 Å, ε 11,600 in EtOH ; Cope *et al.*, *Org. Synth.*, 1951, **31**, 25) was converted by heating with copper powder and either pyridine or collidine into *cyclo*hexenylacetonitrile (88%), b. p. 96—98°/10 mm., n_D^{22} 1·4775, $\lambda_{max.}$ <2100 Å, which was isomerised by 0·1N-sodium ethoxide in ethanol at room temperature into *cyclo*hexylideneacetonitrile (83%), b. p. 98—100°/12 mm., n_D^{23} 1·4890, $\lambda_{max.}$ 2170 Å, ε 13,700 in EtOH (cf. Kandiah and Linstead, *J.*, 1929, 2139).

To a stirred solution of the nitrile (10 g.) in ether (100 ml.) was added lithium aluminium hydride (1·0 g.) in ether (50 ml.) at −50° under nitrogen. After 20 min., ice-cold 2N-sulphuric acid was added. Isolation of the ether-soluble products (which did not give a precipitate with Brady's reagent) and fractionation furnished a mixture (7·5 g.) of *cyclo*hexylacetonitrile and unchanged starting material, b. p. 94—97°/10 mm., n_D^{25} 1·4710, $\lambda_{max.}$ 2150 Å, ε 9000 in EtOH

* We are much indebted to Professor E. R. H. Jones, F.R.S., for communicating this method to us in advance of publication.

(Found : C, 78·7; H, 10·6; N, 11·6. Calc. for $C_8H_{13}N$: C, 78·0; H, 10·6; N, 11·4. Calc. for $C_8H_{11}N$: C, 79·3; H, 9·2; N, 11·6%). Reduction at −20° for 3 hr. gave a lower yield (3·8 g.) of products of similar composition, together with much polymeric material.

The nitrile mixture (4·5 g.) was hydrolysed at 130—140° with 90% phosphoric acid (20 ml.) for 5 hr. Extraction of the products with ether gave crude *cyclo*hexylacetic acid (1·1 g.) which was converted into the amide, m. p. 169—170°, undepressed on admixture with an authentic specimen (Wallach, *Annalen*, 1907, **353**, 297, gives m. p. 168°).

*Reduction of Cyano*cyclo*hexene*.—Cyano*cyclo*hexene (10·7 g.; b. p. 84—85°/15 mm., n_D^{19} 1·4810, $\lambda_{max.}$ 2110 Å, ε 11,200 in EtOH; prepared by dehydration of *cyclo*hexanone cyanohydrin) was reduced with lithium aluminium hydride (1·1 g.) in ether as above. Isolation of the products gave a mixture of cyano*cyclo*hexane and unchanged starting material, b. p. 67—69°/10 mm., n_D^{20} 1·4660, $\lambda_{max.}$ 2130 Å, ε 4000 in EtOH. This was hydrolysed with 90% phosphoric acid at 100° for 12 hr. and the crude acid was converted into the amide which crystallised from water in plates, m. p. 185—186° (Lumsden, *J.*, 1905, 90, gives m. p. 185—186°), undepressed on admixture with an authentic specimen of the derivative of *cyclo*hexanecarboxylic acid, prepared by carboxylation of *cyclo*hexylmagnesium bromide (cf. Gilman and Parker, *Org. Synth.*, 1925, **5**, 75).

2′-*Methyl*cyclo*hexylideneacetaldehyde* (I*b*).—Freshly distilled 2-methyl*cyclo*hexanone (11·2 g.) and allyl chloride (7·7 g.) in ether (500 ml.) and benzene (200 ml.) were added during 3 hr. to magnesium (2·4 g.) and a trace of iodine in ether (100 ml.). After being heated under reflux for an extra ½ hr., the mixture was cooled to 0°, and excess of ice-cold 2N-sulphuric acid was added. Isolation of the ether-soluble products and fractionation gave some unchanged ketone (1·5 g.) and 1-*allyl*-2-*methyl*cyclo*hexanol* (11·0 g., 70%), b. p. 70—75°/10 mm., n_D^{20} 1·469—1·478, presumably as a mixture of *cis*- and *trans*-isomers (Found : C, 77·8; H, 11·7. $C_{10}H_{18}O$ requires C, 77·9; H, 11·8%).

The alcohol, in batches of 10 g., was ozonised in acetic acid (50 ml.) at 0° until absorption ceased (12 hr.). The product was worked up as described on p. 325, giving the crude aldehyde (4·3 g., 60%), b. p. 100—120°/10 mm., $\lambda_{max.}$ 2320 Å, ε 6000 in hexane. Refractionation from powdered potassium hydrogen sulphate (0·4 g.) gave as the main product 2′-*methyl*cyclo*hexylideneacetaldehyde*, b. p. 99—100°/10 mm., n_D^{20} 1·4930, $\lambda_{max.}$ 2300 Å, ε 12,000 in hexane (Found : C, 75·9; H, 10·2. $C_9H_{14}O$ requires C, 78·2; H, 10·2%). The *semicarbazone* crystallised from aqueous ethanol in plates, m. p. 204°, $\lambda_{max.}$ 2740 Å, ε 28,000 in EtOH (Found : C, 61·8; H, 8·9; N, 21·2. $C_{10}H_{17}ON_3$ requires C, 61·5; H, 8·8; N, 21·5%). The 2 : 4-*dinitrophenylhydrazone* was chromatographed on alumina in benzene and crystallised from ethanol–ethyl acetate in plates, m. p. 174°, $\lambda_{max.}$ 3840 Å, ε 28,000 in $CHCl_3$ (Found : C, 57·1; H, 5·8; N, 17·5. $C_{15}H_{18}O_4N_4$ requires C, 56·6; H, 5·7; N, 17·6%).

From the lower-boiling fractions, b. p. 80—90°/10 mm., n_D^{24} 1·470—1·479, the *semicarbazone* of 2′-methyl*cyclo*hexenylacetaldehyde was obtained and crystallised from ethanol in fine needles, m. p. 204° (mixed m. p. with the semicarbazone of 2′-methyl*cyclo*hexylideneacetaldehehyde, 190°), $\lambda_{max.}$ 2330 Å, ε 15,400 in EtOH (Found : C, 61·3; H, 8·9; N, 21·4. $C_{10}H_{17}ON_3$ requires C, 61·5; H, 8·8; N, 21·5%).

Redistillation of the higher-boiling fractions gave 1′-*hydroxy*-2′-*methyl*cyclo*hexylacetaldehyde* as a highly viscous oil, b. p. 98—100°/0·5 mm. (Found : C, 69·3; H, 9·8. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%). On treatment with Brady's reagent it formed the 2 : 4-dinitrophenylhydrazone of 2′-methyl*cyclo*hexylideneacetaldehyde, m. p. 174°, undepressed on admixture with the specimen described above.

1-cyclo*Hex*-1′-*enyl*-2-cyclo*hexylidene-ethanol* (II*a*).—*cyclo*Hexylideneacetaldehyde (6 g.) in ether (60 ml.) was added during 30 min. to *cyclo*hexenyl-lithium (from 1-chloro*cyclo*hexene, 6·4 g., and lithium, 0·7 g.; cf. *J.*, 1950, 2014) in ether (100 ml.) under nitrogen at room temperature. Stirring was continued for a further 30 min. and then excess of ice-cold saturated aqueous ammonium chloride was added at 0°. The ether layer was separated, dried (Na_2SO_4–K_2CO_3) and distilled from a trace of potassium carbonate, giving 1-cyclo*hex*-1′-*enyl*-2-cyclo*hexylidene-ethanol* (3·6 g., 36%), b. p. 100° (bath-temp.)/10^{-4} mm., n_D^{20} 1·5225 (Found : C, 81·3; H, 10·6. $C_{14}H_{22}O$ requires C, 81·5; H, 10·8%).

1-(2-cyclo*Hex*-1′-*enylvinyl*)cyclo*hexanol* (III*a*).—The above alcohol (3 g.) was dissolved in a 0·001M-solution of hydrogen chloride in 75% aqueous acetone (200 ml.), and the mixture kept at room temperature under nitrogen for 15 min. Excess of aqueous potassium carbonate was then added, the acetone was removed under reduced pressure, and the aqueous residue extracted with ether. The ether layer was separated, washed with water, dried (K_2CO_3), and distilled, giving 1-(2-cyclo*hex*-1′-*enylvinyl*)cyclo*hexanol* (2·3 g.), b. p. 80° (bath-temp.)/10^{-4} mm., n_D^{19}

1·5360, $\lambda_{max.}$ 2360 Å, ε 18,000 in EtOH (Found: C, 81·4; H, 11·0. $C_{14}H_{22}O$ requires C, 81·5; H, 10·75%). When the alcohol (300 mg.) was kept with maleic anhydride (160 mg.) in benzene (1·5 ml.) overnight at room temperature, the *adduct* (80 mg.) was precipitated; it crystallised from benzene in plates, m. p. 198° (Found: C, 71·5; H, 7·9. $C_{18}H_{24}O_4$ requires C, 71·0; H, 8·0%).

1 : 2-*Dicyclohex-1'-enylethylene* (IV*a*).—The foregoing alcohol (1·8 g.) was distilled rapidly from powdered potassium hydrogen sulphate (0·8 g.) at 10^{-4} mm. The product was redistilled and had b. p. 100°/10^{-4} mm., n_D^{22} 1·5670, $\lambda_{max.}$ 2590 (ε 22,000), 2680 (ε 27,000), and 2800 Å (ε 24,000) in EtOH (Found: C, 87·3; H, 10·8; O, 3·4. Calc. for $C_{14}H_{20}$: C, 89·3; H, 10·7. Calc. for $C_{14}H_{20}O_2$: C, 76·3; H, 9·2; O, 14·5%). Even on brief exposure to air, the oxygen content increased markedly. If the oxygen is assumed to be bound in the proportions indicated, the analytical results above correspond to a triene content of 75%, and to an ε_{2680} value of 36,000 for the pure triene (Burkhardt and Hindley, *J.*, 1938, 987, report $\lambda_{max.}$ 2690 Å, ε 42,000). No adduct was obtained with maleic anhydride in benzene at room temperature.

1-cyclo*Hex*-1'-*enyl*-2-(2-*methyl*cyclo*hexylidene*)*ethanol* (II*b*).—2'-Methyl*cyclo*hexylideneacetaldehyde (6·2 g.) in ether (50 ml.) was added to *cyclo*hexenyl-lithium (from 1-chloro*cyclo*hexene, 5·8 g., and Li, 1·4 g.) in ether (100 ml.) at 0°. Stirring was continued for 30 min. at room temperature and then excess of ammonium chloride was added at 0°. The product was worked up as above, giving the *alcohol* (3·3 g., 33%), b. p. 100° (bath-temp.)/10^{-4} mm., n_D^{20} 1·5150 (Found: C, 81·4; H, 10·9. $C_{15}H_{24}O$ requires 81·8; H, 11·0%).

1-(2-2'-*Methyl*cyclo*hex*-1'-*enylvinyl*)cyclo*hexanol* (III*b*).—The foregoing alcohol (3 g.) was added to a 0·002M-solution of hydrogen chloride in 80% aqueous acetone (200 ml.) and the mixture kept for 20 min. at room temperature. Excess of potassium carbonate was then added and the product worked up as above, giving the *alcohol* (2·1 g.), b. p. 100° (bath-temp.)/10^{-4} mm., n_D^{24} 1·5230, $\lambda_{max.}$ 2370 Å, ε 15,000 in EtOH (Found: C, 81·1; H, 11·0. $C_{15}H_{24}O$ requires C, 81·8; H, 11·0%).

1-cyclo*Hexenyl*-2-(2-*methyl*cyclo*hex*-1-*enyl*)*ethylene* (IV*b*).—The foregoing alcohol (1·7 g.) was distilled from powdered potassium hydrogen sulphate (0·5 g.) at 10^{-4} mm. Redistillation gave a product (1·2 g.), b. p. 105—107°/10^{-4} mm., n_D^{21} 1·5415, $\lambda_{max.}$ 2710 (ε 20,000) and 2810 Å (ε 29,500) in EtOH (Found: C, 84·3; H, 10·9; O, 5·3. Calc. for $C_{15}H_{22}$: C, 89·0; H, 11·0. Calc. for $C_{15}H_{22}O_2$: C, 76·9; H, 9·4; O, 13·7%). The analytical data correspond to a triene content of 60% and to an ε_{2710} value of 34,000 for the pure triene. No adduct was obtained with maleic anhydride in benzene at room temperature.

1-cyclo*Hexenylidene*-2-(1-*methyl*cyclo*hex*-1-*enylidene*)*ethane*.—*cyclo*Hexylideneacetaldehyde (2 g.) was added during 3 hr. with vigorous shaking, to *cyclo*hexanone (5 g.) and 0·05N-sodium hydroxide (200 ml.) under nitrogen. The condensation product (2 g.) was isolated with ether, distilled at 10^{-4} mm., and finally crystallised from ethanol as needles, m. p. 65°, $\lambda_{max.}$ 3070 Å, ε 20,000 in EtOH (Dimroth, *Ber.*, 1938, **71**, 1346, gives m. p. 67°, $\lambda_{max.}$ 2970 Å, ε 25,000 in Et_2O). The 2 : 4-*dinitrophenylhydrazone* was chromatographed on alumina in benzene and crystallised from ethyl acetate as dark red needles, m. p. 206°, $\lambda_{max.}$ 3150 (ε 14,000) and 4200 Å (ε 21,000) in $CHCl_3$ (Found: C, 62·3; H, 6·4; N, 14·6. $C_{20}H_{24}O_4N_4$ requires C, 62·5; H, 6·3; N, 14·6%).

The ketone was allowed to react with methylmagnesium bromide (2 mols.) in ether, and the product was hydrolysed with aqueous ammonium chloride, and the resulting tertiary alcohol was isolated from the ether layer. The crude alcohol (0·4 g.; $\lambda_{max.}$ 2480 Å, ε 18,000 in EtOH) was added to pyridine (4 ml.) and toluene-*p*-sulphonyl chloride (200 mg.) and the mixture heated at 80° for 5 min. under nitrogen. After dilution with ice and hydrochloric acid, the product was isolated with ether, giving a triene (0·26 g.), b. p. 100°/10^{-3} mm., $\lambda_{max.}$ 2820 Å, ε 20,000 in EtOH (Dimroth, *loc. cit.*, gives $\lambda_{max.}$ 2760 Å, ε 23,000 in Et_2O). A similar result was obtained with phosphorus oxychloride in pyridine as dehydrating agent.

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Studies in the Vitamin D Field. Part II. The Condensation of Acetylmethylcyclohexenes with cycloHexanone.*

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The condensation of 1-acetyl-2-methyl*cyclo*hexene (Ib) with *cyclo*hexanone, previously studied by Huber and by Turner and Voitle, has been re-investigated and found to give bicyclic as well as tricyclic products. Reduction of the bicyclic product (VI*b*) with lithium aluminium hydride yields the diethylenic alcohol (VII*b*). The monoallylic rather than diallylic structure of the latter is indicated by the relatively slow rate of its acid-catalysed anionotropic rearrangement which is accompanied by dehydration to diconjugated trienes and cyclisation. This approach does not, therefore, provide a useful route to the desired triconjugated trienes.

2-Acetyl-3-methyl*cyclo*hexene (I*c*) has been synthesised by an unambiguous method and has been found to undergo analogous reactions.

In Part I *, a new route to tachysterol analogues has been outlined. A possible alternative method of obtaining the diene alcohols required as intermediates consists of the selective reduction of the corresponding diene ketones. One such ketone (IV*b*) is theoretically accessible by the condensation of 1-acetyl-2-methyl*cyclo*hexene (I*b*) with *cyclo*hexanone. This reaction was first investigated by Huber (*Ber.*, 1938, **71**, 725) who, using potassium *iso*propoxide as catalyst, obtained as the sole product a tricyclic ketone regarded as (III*b*) and presumably formed *via* (II*b*) by successive Michael addition and internal condensation, as observed with 1-acetyl*cyclo*hexene (I*a*) (Rapson and Robinson, *J.*, 1935, 1285). More recently, the condensation of 1-acetyl-2-methyl*cyclo*hexene with *cyclo*hexanone under slightly different conditions (potassium *tert.*-butoxide) was re-investigated by Turner and Voitle (*J. Amer. Chem. Soc.*, 1950, **72**, 4166) who reported that the reaction did not furnish the tricyclic ketone, but gave a mixture of diethylenic ketones whose skeletal structure was proved to correspond to (IV*b*), though the position of the double bonds was not conclusively established.

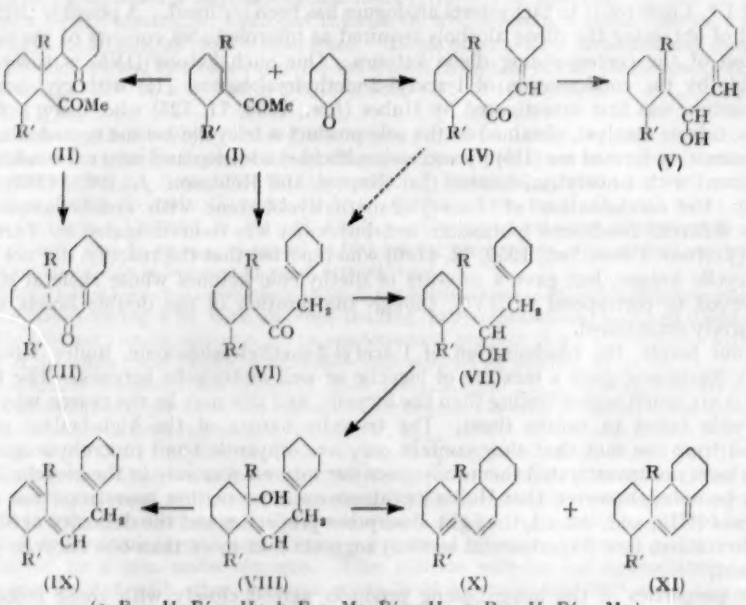
In our hands, the condensation of 1-acetyl-2-methyl*cyclo*hexene, under Turner and Voitle's conditions, gave a mixture of bicyclic as well as tricyclic ketones. The tricyclic products are much higher-boiling than the bicyclic, and this may be the reason why Turner and Voitle failed to isolate them. The tricyclic nature of the high-boiling products followed from the fact that they contain only *one* ethylenic bond (microhydrogenation), but we have not investigated them fully since our interest was only in the bicyclic ketones. It may be noted, however, that Huber's evidence excludes neither prototropic nor skeletal isomers of (III*b*) and, indeed, the light-absorption properties and the difficulty of obtaining solid derivatives (see Experimental section) suggests that more than one tricyclic product is present.

The properties of the lower-boiling products agreed closely with those recorded by Turner and Voitle. The ultra-violet and infra-red light-absorption properties ($\lambda_{max.}$ 2470 Å, ε 5500; $\nu_{max.}$ 1680 cm.$^{-1}$) indicate a predominance of the monoconjugated ketone (VI*b*), the low intensity of the ultra-violet band being ascribed to steric hindrance to uniplanarity of the enone system, as in 1-acetyl-2-methyl*cyclo*hexene (I*b*) ($\lambda_{max.}$ 2450, ε 6500; $\nu_{max.}$ 1686 cm.$^{-1}$; Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890; Henbest and Woods, *J.*, 1952, 1150). The maximum of the diconjugated ketone (IV*b*) should be located near 2550 Å (cf. phorone, $\lambda_{max.}$ 2580 Å, ε 20,000 in EtOH), and although some (IV*b*) was probably present its proportion was evidently so low as to cause only band-broadening on the long-wave-length side.

Reduction of the ketone (VI*b*) with lithium aluminium hydride furnished the diethylenic

* Part I, preceding paper.

alcohol (VII*b*) which is transparent in the near-ultra-violet and undergoes no significant change in the presence of 0·001M-hydrogen chloride in aqueous dioxan at room temperature. This confirms that no appreciable amount of the diallylic alcohol (V*b*) which undergoes rapid anionotropic rearrangement under such conditions (Part I; cf. Braude, *Quart. Reviews*, 1950, **4**, 404) was present. As expected for a monoallylic alcohol, (VII*b*) was isomerised only under much more strongly acid conditions (0·1N-hydrogen chloride). Rearrangement to (VIII*b*) was accompanied by extensive dehydration and by the appearance of two absorption bands near 2400 and 2800 Å, the relative intensities of which were very dependent on the acid catalyst employed (see Experimental section). The two bands could be due, respectively, to the diconjugated* triene (IX*b*) and the corresponding triconjugated triene, the isolated double bond having been moved into the conjugated position under the influence of the acid catalyst. Microhydrogenation, however, showed the presence of only *two* double bonds indicating that acid-catalysed cyclisation had taken place and that the 2400-Å maximum belongs to a tricyclic diene (*e.g.*, X*b*) and the 2800-Å band to an isomeric tricyclic diene (XI*b*) containing the ergosterol type of chromophoric system. The formulations (X*b*) and (XI*b*) are supported both by the low intensities of the bands, and by the formation, presumably from (XI*b*), of a maleic anhydride adduct, isolated as the crystalline *N*-phenylimide.

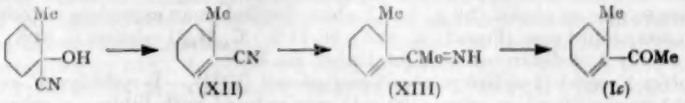


(*a*, R = H, R′ = H; *b*, R = Me, R′ = H; *c*, R = H, R′ = Me.)

Since 1-acetyl-2-methyl*cyclo*hexene is known to undergo quite rapid prototropic isomerisation under the influence of metal alkoxides (cf. Braude *et al.*, *loc. cit.*, 1949), the corresponding sequence of reactions was, for comparison, carried through with 2-acetyl-3-methyl*cyclo*hexene (I*c*). This compound was obtained by Dimroth and Lüderitz (*Chem. Ber.*, 1947, **81**, 242), together with 1-acetyl-2-methyl*cyclo*hexene, by the treatment of 1-ethynyl-2-methyl*cyclo*hexanol with formic acid. The separation of the two products was, however, incomplete, and the assigned constitution was based solely on spectroscopic evidence. 2-Acetyl-3-methyl*cyclo*hexene has now been prepared by an unambiguous route, starting

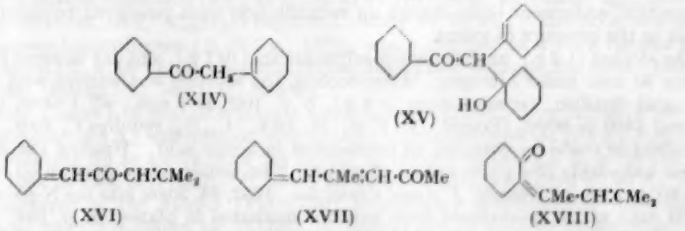
* Diconjugated and triconjugated refer to the structures having two and three double bonds in conjugation.

with the cyanohydrin of 2-methyl*cyclo*hexanone which was dehydrated by phosphorus oxychloride in pyridine to 2-cyano-3-methyl*cyclo*hexene (XII). The constitution of the latter was established by hydrolysis to 6-methyl*cyclo*hex-1-ene-1-carboxylic acid (Rapson and Shuttleworth, *J.*, 1940, 636) and by its ultra-violet light absorption ($\lambda_{max.}$ 2100, ε 9500), typical of the C:C·C:N system (cf. 1-cyano*cyclo*hexene, $\lambda_{max.}$ 2110 Å, ε 11,000; Part I, *loc. cit.*). Reaction of the cyanide with methylmagnesium iodide in benzene at 80°, followed by hydrolysis with dilute hydrochloric acid, gave the ketimine (XIII) characterised by a picrate. The ketimine shows a resistance to hydrolysis similar to that of aromatic ketimines (cf. Pickard *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 42; 1952, **74**, 4607; 1953, **75**, 5899; Culbertson, *ibid.*, 1951, **73**, 4818), but it is converted by hot hydrochloric or sulphuric acids into the ketone (I*c*) which was characterised by a semicarbazone. In contrast to 1-acetyl-3-methyl*cyclo*hexene, 2-acetyl-3-methyl*cyclo*hexene, and its derivatives exhibit almost normal spectroscopic properties, as would be expected since even in 2-acetyl-3 : 3-dimethyl*cyclo*hexene steric hindrance to the planarity of the conjugated enone system is only slight (Braude *et al.*, *loc. cit.*, 1949).



Condensation of 2-acetyl-3-methyl*cyclo*hexene with *cyclo*hexanone under the same conditions as those used for 1-acetyl-2-methyl*cyclo*hexene again gave two products differing widely in boiling point and shown by microhydrogenation to be diethylenic and monoethylenic, respectively. The higher-boiling monoethylenic, tricyclic ketone (III*c*) was not further investigated. Reduction of the lower-boiling, diethylenic, bicyclic ketone (VI*c*) gave the alcohol (VII*c*) which like the isomer (VII*b*) underwent rearrangement and dehydration on acid treatment to a mixture of readily oxidised hydrocarbons, probably mainly (X*c*) and (XI*c*).

For further comparison, the condensation of certain related ketones with *cyclo*hexanone under similar conditions has also been studied. Acetyl*cyclo*hexane gave the unconjugated *cyclo*hexenylacetyl*cyclo*hexane (XIV), characterised as the semicarbazone and 2 : 4-dinitrophenylhydrazone, together with a solid product, probably (XV) derived from 1 mol. of acetyl*cyclo*hexane and 2 mols. of *cyclo*hexanone. On the other hand, mesityl oxide which represents an acyclic analogue of acetylmethyl*cyclo*hexene, gives a diene ketone the spectral properties of which ($\lambda_{max.}$ 2950 Å, ε 14,500) show that it is not the cross-conjugated analogue (XVI), but must have either the structure (XVII) or (XVIII). The ultra-violet absorption makes (XVIII), which contains a *cisoid* enone grouping, more probable and it appears that the keto-group of mesityl oxide is relatively more reactive in this type of condensation than that of the acetyl*cyclo*hexenes.



Experimental

For general methods, see Part I, *loc. cit.* Light-absorption data refer to ethanol solutions unless otherwise stated. Microhydrogenations were done in acetic acid, with platinic oxide as a catalyst.

Condensation of 1-*Acetyl-2-methyl*cyclo*hexene with* cyclo*Hexanone.*—1-Acetyl-2-methyl*cyclo*-

hexene (10 g.; n_D^{22} 1·869; $\lambda_{max.}$ 2420 Å, ε 5500; prepared from either 1-methyl*cyclo*hexene or 1-ethynyl*cyclo*hexanol and purified by way of the semicarbazone as described by Braude *et al.*, *J.*, 1949, 1890), *cyclo*hexanone (7 g.), and dry pyridine (25 ml.) was added slowly to a solution prepared from potassium (3·5 g.), dry *tert.*-butanol (30 ml.), and ether (50 ml.). The mixture rapidly became homogeneous and assumed an orange colour, and a precipitate was slowly deposited. After 3 days at room temperature, water was added, the two layers were separated, the aqueous layer was acidified at 0° with hydrochloric acid and extracted with ether, and the combined ethereal solutions were washed with 2N-hydrochloric acid, 2N-sodium hydroxide, and water, and dried (Na_2SO_4). Distillation afforded two main fractions : (i) 1-cyclo*hex*-1′-*enylacetyl*-2-*methyl*cyclo*hexene* (8·0 g., 50%), b. p. 105—106°/0·005 mm., n_D^{20} 1·5164, $\lambda_{max.}$ 2470 Å, ε 5500 (Found : C, 81·8; H, 10·2. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%. Microhydrogenation no. 94. Calc. for 2 double bonds, 109); (ii) a mixture of decahydromethyloxophenanthrenes (?) (3·5 g., 22%) which distilled as a very viscous oil, b. p. 90° (bath-temp.)/10^{-4} mm., n_D^{20} 1·5310, $\lambda_{max.}$ 2360 ε 3400 (Found : C, 81·9; H, 10·3. Microhydrogenation no., 200. Calc. for one double bond, 218). The 2 : 4-dinitrophenylhydrazones prepared from both fractions were oils (cf. Huber, *Ber.*, 1938, **71**, 725; Turner and Voitle, *J. Amer. Chem. Soc.*, 1950, **72**, 4166).

Fraction (ii) was reduced with lithium aluminium hydride (0·75 g.) in ether at room temperature to give an *alcohol* (2·9 g., 80%) which distilled as an extremely viscous glass, b. p. 100° (bath-temp.)/10^{-4} mm. (Found : C, 81·5; H, 11·3. $C_{15}H_{24}O$ requires C, 81·8; H, 11·0%), and gave an oily 3 : 5-dinitrobenzoate (cf. Huber, *loc. cit.*).

2-cyclo*Hex*-1′-*enyl*-1-(2-*methyl*cyclo*hex*-1-*enyl*)*ethanol* (VII*b*).—1-*cyclo*Hex-1′-enylacetyl-2-methyl*cyclo*hexene (8·0 g.) in ether (100 ml.) was reduced with lithium aluminium hydride (1·6 g.) in ether (100 ml.) at −25°. After hydrolysis with aqueous ammonium chloride, the ether layer was separated, dried (Na_2SO_4–K_2CO_3), and distilled, giving the *alcohol* as a colourless, very viscous oil (7·3 g., 90%), b. p. 105—107°/10^{-3} mm., n_D^{25} 1·5170, ε < 1000 at 2470 Å (Found : C, 81·5; H, 11·2%).

Acid Treatment of the Alcohol (VII*b*).—(i) Preliminary experiments were carried out by adding 0·1 ml. of a stock solution of the foregoing alcohol (1·85 mg.) in purified dioxan (10 ml.) to solutions of hydrogen chloride in 60% aqueous dioxan (2·5 ml.) contained in the 1-cm. cell of a Unicam S.P.500 spectrophotometer and observing the change in ultra-violet light absorption (cf. Barany, Braude, and Coles, *J.*, 1951, 2093). No significant change was observed with 0·001M-hydrochloric acid during 24 hr. at 25°, and only very slow change with 0·01M-acid. With 0·1M-acid, the following results, typical of several runs, were obtained :

Time (min.)	0	25	50	75	90	120	235
ε_{2400} (Å)	120	1600	3000	4300	5100	6300	9500
ε_{2300} (Å)	50	1200	1400	1700	1800	2000	2500

(ii) The alcohol (6 g.) was dissolved in a 0·1M-solution of hydrogen chloride in 80% aqueous acetone. An oil separated slowly from the initially homogeneous mixture. After 12 hr. at room temperature, the acid was neutralised with potassium carbonate and most of the acetone removed under reduced pressure. Extraction of the residue with ether and distillation gave a *diene* (5·2 g.), b. p. 92—94°/10^{-2} mm., n_D^{23} 1·5380, $\lambda_{max.}$ 2400 Å (ε 13,000) and 2780 Å (ε 5000) which avidly absorbed oxygen (Found : C, 86·7; H, 11·0. $C_{15}H_{22}$ requires C, 89·0; H, 11·0. Microhydrogenation number, 113. Calc. for two double bonds, 101). The physical properties and composition underwent little change on redistillation from powdered potassium hydrogen sulphate or in the presence of iodine.

(iii) The alcohol (1·2 g.), naphthalene-β-sulphonic acid (0·1 g.), and dry benzene (15 ml.) were refluxed for 30 min. under nitrogen. After cooling, the solution was washed with water, dried (Na_2SO_4), and distilled, giving a *diene* (0·8 g.), b. p. 100°/10^{-2} mm., n_D^{26} 1·5480, $\lambda_{max.}$ 2400 Å, (ε 4000) and 2800 (ε 9000) (Found : C, 87·0; H, 10·8. $C_{15}H_{22}$ requires C, 89·0; H, 11·0%). No formaldehyde could be detected on ozonisation in acetic acid. Heating the diene (1·0 g.) with maleic anhydride (0·4 g.) in xylene (2 ml.) for 2 hr. under reflux gave an oil converted by aniline at 90° in 1 hr. (cf. Conroy, *J. Amer. Chem. Soc.*, 1952, **74**, 3046) into the N-*phenylmaleimide* adduct (70 mg.) which crystallised from aqueous methanol in plates, m. p. 194° (Found : C, 78·9; H, 7·6; N, 4·3; O, 9·55. $C_{25}H_{29}NO_2.\frac{1}{2}H_2O$ requires C, 78·9; H, 7·8; N, 3·7; O, 9·8%).

2-*Acetyl*-3-*methyl*cyclo*hexene* (I*c*).—Liquid hydrogen cyanide (100 ml.) and a few crystals of potassium cyanide were added to 2-methyl*cyclo*hexanone (135 g.), and the mixture kept in a stoppered flask for 2 days at room temperature. Syrupy phosphoric acid (2 ml.) was then added until the mixture was acid to methyl-orange. The excess of hydrogen cyanide was removed under reduced pressure, and the residue distilled, giving unchanged ketone (20 g.), b. p. 55—

58°/0·2 mm., and the cyanohydrin (128 g.), b. p. 70—72°/0·5 mm., n_D^{21} 1·4640 (Linstead and Millidge, *J.*, 1936, 482, give b. p. 122°/10 mm.). The cyanohydrin was also prepared, in similar yield, by adding concentrated hydrochloric acid to a mixture of ketone and potassium cyanide below 0° (cf. Billimoria and Maclagan, *J.*, 1951, 3069).

The cyanohydrin (25 g.) was dehydrated by treatment with phosphorus oxychloride (30 ml.) and dry pyridine (30 ml.), the reactants being mixed at 0° and then kept at 20° for 20 min. and finally at 90° for 30 min. After cooling, ice was added and the ethereal layer was separated, washed with hydrochloric acid, dried, and distilled, giving 2-cyano-3-methyl*cyclo*hexene (17 g., 77%), b. p. 78°/10 mm., n_D^{21} 1·4782, $\lambda_{max.}$ 2100 Å, ε 9500 (Linstead and Millidge, *loc. cit.*, give b. p. 86°/10 mm.). A small portion was hydrolysed by heating with phosphoric acid (90%) at 130—140° for 5 hr. to 6-methyl*cyclo*hex-1-ene-1-carboxylic acid, m. p. 104°, $\lambda_{max.}$ 2160 Å, ε 10,500 (Rapson and Shuttleworth, *J.*, 1940, 636, give m. p. 105°).

Methylmagnesium iodide (from Mg, 3 g., and MeI, 20 g.) was prepared in ether (50 ml.), benzene (50 ml.) was added, and the ether distilled off by heating until the vapour temperature reached 70°. 2-Cyano-3-methyl*cyclo*hexene (10 g.) was then added at 20° and the mixture refluxed for 6 hr. (cf. Haworth and Mavin, *J.*, 1932, 2720; Fieser and Seligman, *J. Amer. Chem. Soc.*, 1936, **58**, 2482). After cooling, excess of aqueous ammonium chloride was added and the ether layer was separated and extracted with 5% aqueous sulphuric acid at 0°. The acidic extract was immediately poured into excess of aqueous ammonia and the oil which separated was taken up in ether and dried (Na_2SO_4). Distillation gave the unstable 2-*acetyl*-3-*methyl*cyclo*hexene ketimine* (5·9 g., 58%), b. p. 38°/0·2 mm., n_D^{24} 1·4975, $\lambda_{max.}$ 2270 Å, ε 5500 (Found: C, 78·5; H, 11·2; N, 9·8. $C_9H_{15}N$ requires C, 78·8; H, 11·0; N, 10·2%). The *picrate* crystallised from benzene in plates which had a double m. p. 112° and 122° (Found: C, 48·5; H, 5·3; N, 15·9. $C_{15}H_{18}O_7N_4$ requires C, 49·2; H, 5·0; N, 15·3%).

Hydrolysis of the ketimine (4·0 g.) was effected by heating with N-sulphuric acid (100 ml.) and benzene (20 ml.) under reflux for 15 min. Distillation of the benzene layer gave 2-*acetyl*-3-*methyl*cyclo*hexene* (3·1 g.), b. p. 90°/15 mm., n_D^{20} 1·4875, $\lambda_{max.}$ 2340 Å, ε 11,000 (Found: C, 77·5; H, 10·2. $C_9H_{14}O$ requires C, 78·2; H, 10·2%) (Dimroth and Lüderitz, *loc. cit.*, give $\lambda_{max.}$ 2380 Å, ε 8300, but no analytical data). The *semicarbazone* was crystallised from ethanol and had m. p. 204°, $\lambda_{max.}$ 2580 Å, ε 22,000 (Found: C, 61·7; H, 8·6; N, 21·1. $C_{10}H_{17}ON_3$ requires C, 61·5; H, 8·8; N, 21·5%) (Dimroth and Lüderitz, *loc. cit.*, give m. p. 208° for a derivative which was formulated as a pyrazoline but was almost certainly the semicarbazone; cf. Braude *et al.*, *J.*, 1949, 1890). The 2 : 4-*dinitrophenylhydrazone* was chromatographed on alumina in benzene and crystallised from methanol in plates, m. p. 132°, $\lambda_{max.}$ 3860 Å, ε 23,000 in $CHCl_3$ (Found: C, 56·7; H, 5·9; N, 17·8. $C_{15}H_{18}O_4N_4$ requires C, 56·6; H, 5·7; N, 17·6%).

In subsequent experiments, the ketone was obtained directly from the Grignard reaction mixture by hydrolysis with concentrated hydrochloric acid (5 ml.) at 80° for 20 min. The yield was 6·8 g. (63%). When the time of reflux with methylmagnesium iodide was reduced to 1 hr., the yield dropped to 38%. Mainly unchanged nitrile and a very low yield of ketone (5%, isolated as the semicarbazone) were obtained from a Grignard reaction in refluxing ether. No appreciable reaction took place in ether at room temperature.

Condensation of 2-*Acetyl*-3-*methyl*cyclo*hexene with* cyclo*Hexanone*.—2-Acetyl-3-methyl*cyclo*hexene (8·1 g.) was condensed with *cyclo*hexanone (6·4 g.) under the same conditions as described above for 1-acetyl-2-methyl*cyclo*hexene. Two main products were obtained: (i) 2-cyclo*hex*-1′-*enylacetyl*-3-*methyl*cyclo*hexene* (6 g., 46%), b. p. 97°/10^{-3} mm., n_D^{18} 1·5240, $\lambda_{max.}$ 2430 Å, ε 5700 (Found: C, 82·4; H, 10·2. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%); and (ii) a mixture of decahydromethyloxophenanthrenes (?) (2·5 g., 19%), which distilled as a very viscous glass, b. p. 100° (bath-temp.)/5 × 10^{-4} mm., showing diffuse absorption through the 2300—2600-Å region (ε 2000—3000) (Found: C, 80·5; H, 10·2%).

2-cyclo*Hex*-1′-*enyl*-1-(6-*methyl*cyclo*hex*-1-*enyl*)*ethanol* (VII*c*).—2-*cyclo*Hex-1′-enylacetyl-3-methyl*cyclo*hexene (4·4 g.) was reduced with lithium aluminium hydride (0·9 g.) in ether (60 ml.) at −20°. Working up as above gave the *alcohol* as viscous oil (4·0 g.), b. p. 98°/10^{-3} mm., n_D^{22} 1·5230, ε <1000 at 2400 Å (Found: C, 81·4; H, 11·1. $C_{15}H_{24}O$ requires C, 81·8; H, 11·0%).

Acid Treatment of the Alcohol (VII*c*).—(i) Preliminary spectrometric experiments were carried out as described above for (VII*b*). A typical run in 0·1M-hydrogen chloride in 60% aqueous dioxan at 20° was as follows:

Time (min.)	25	50	90	135	240
ε_{2380} (Å)	2700	3500	4500	5400	6800
ε_{1900} (Å)	1300	1600	1800	2000	2300

(ii) The alcohol (3·5 g.) was dissolved in 0·1M-hydrogen chloride in 80% aqueous acetone (200 ml.), and the mixture kept at room temperature for 18 hr. Isolation of the product as previously gave a viscous oil (2·9 g.), b. p. 88°/10^{-3} mm., n_D^{20} 1·5338, $\lambda_{max.}$ 2380 (ε 9000) and 2800 Å (ε 3000) (Found : C, 85·5; H, 11·0. $C_{15}H_{22}$ requires C, 89·0; H, 11·0%). Redistillation from potassium hydrogen sulphate gave a *diene* (1·7 g.), b. p. 88°/10^{-3} mm., n_D^{22} 1·5335 (Found : C, 86·3; H, 11·0. Microhydrogenation no. 98. Calc. for 2 double bonds, 101), which rapidly absorbed oxygen (Found : O, 6·2% after 4 hr.; 7·6% after 20 hr.). The oxygen was only partly removed by distillation from zinc dust (Found : C, 85·5; H, 11·0; O, 3·5%).

*Condensation of Acetyl*cyclo*hexane with* cyclo*Hexanone.*—Acetyl*cyclo*hexene (prepared by the method of Deno and Chafetz, *J. Amer. Chem. Soc.*, 1952, **74**, 3940) was hydrogenated in ethyl acetate in the presence of platinic oxide. Distillation gave acetyl*cyclo*hexane, b. p. 70°/12 mm., n_D^{19} 1·4525 (Wieland and Bettag, *Ber.*, 1922, **55**, 2246, give b. p. 74—77°/10 mm.). The 2 : 4-dinitrophenylhydrazone was chromatographed on alumina in benzene and crystallised from ethyl acetate in orange prisms, m. p. 140°, $\lambda_{max.}$ 3680 Å, ε 22,000 in $CHCl_3$ (Found : C, 55·0; H, 6·1; N, 18·1. Calc. for $C_{14}H_{18}O_4N_4$: C, 54·9; H, 5·9; N, 18·3%) (Hughes and Lions, *Proc. Roy. Soc. New South Wales*, 1938, **41**, 494, give m. p. 128°).

Acetyl*cyclo*hexane (6 g.) and *cyclo*hexanone (5 g.) in pyridine (20 ml.) were added to a solution of potassium *tert.*-butoxide (from K, 2·2 g.) in dry *tert.*-butanol (20 ml.) and ether (50 ml.). After 6 days at room temperature, the mixture was worked up in the usual manner and yielded a solid product (4·6 g.) and an oil (2·8 g.). The oil was distilled, giving cyclo*hex*-1′-*enylacetyl*-cyclo*hexane*, b. p. 76°/10^{-3} mm., n_D^{20} 1·5002 (Found : C, 81·0; H, 10·6. $C_{14}H_{22}O$ requires C, 81·5; H, 10·75%). The *semicarbazone* crystallised from aqueous ethanol as needles, m. p. 174°, $\lambda_{max.}$ 2280 Å, ε 13,000 (Found : C, 68·4; H, 9·8; N, 16·1. $C_{15}H_{25}ON_3$ requires C, 68·4; H, 9·6; N, 16·0%). The 2 : 4-*dinitrophenylhydrazone* was chromatographed on alumina in benzene and crystallised from ethyl acetate as yellow prisms, m. p. 102°, $\lambda_{max.}$ 3710 Å, ε 22,000 in $CHCl_3$ (Found : C, 61·8; H, 6·8; N, 14·4. $C_{20}H_{26}O_4N_4$ requires C, 62·1; H, 6·8; N, 14·5%). The solid, formulated as α-cyclo*hex*-1-*enyl*-α-(1-*hydroxy*cyclo*hexyl*)*acetyl*cyclo*hexane* (XV) crystallised from ethyl acetate as needles, m. p. 192°, unchanged after sublimation at 160—180°/0·5 mm. (Found : C, 78·9, 79·1; H, 10·7, 10·7. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%). Ultra-violet light absorption : ε <500 between 2200 and 4000 Å. Infra-red light absorption : $\nu_{max.}$ 1695 cm.$^{-1}$ (ε *ca.* 300, CO stretching) in $CHCl_3$ (10%; NaCl prism) and 3597 cm.$^{-1}$ (ε *ca.* 40, O–H stretching) in CCl_4 (2·5%; LiF prism).

Condensation of Mesityl Oxide with cyclo*Hexanone.*—Mesityl oxide (9·8 g.) was condensed with *cyclo*hexanone (9·8 g.) under the conditions described above for acetylmethyl*cyclo*hexene. Distillation of the products afforded unchanged *cyclo*hexanone (1·5 g.) and 2-(1 : 3-*dimethylbut*-2-*enylidene*)cyclo*hexanone* (?) (6·0 g., 32%), b. p. 75°/0·1 mm., n_D^{19} 1·5220, $\lambda_{max.}$ 2950 Å, ε 14,500, $\lambda_{infl.}$ 3040 Å, ε 13,500 (Found : C, 80·5; H, 10·2. $C_{12}H_{18}O$ requires C, 80·9; H, 10·2%). The 2 : 4-*dinitrophenylhydrazone* was chromatographed on alumina in benzene and crystallised from ethyl acetate as purple needles, m. p. 168° $\lambda_{max.}$ 3070 (ε 16,500) and 4150 Å (ε 27,000), $\lambda_{infl.}$ 4500 Å (ε 20,000) in $CHCl_3$ (Found : C, 60·8; H, 6·6; N, 15·4. $C_{18}H_{22}O_4N_4$ requires C, 60·3; H, 6·2; N, 15·6%).

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The Enrichment of Crude Erbium and Holmium.

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Use of basic nitrates, for which the formula $Ln(NO_3)_3.Ln[LnNO_3(OH)_5].6{\cdot}5$ or $7{\cdot}5H_2O$ is suggested, is considered the best method for enrichment of fractions of erbium and holmium. This and other basic nitrate methods give about the same separation factor, and appear to depend upon the same basic nitrate formation, $Ln[LnNO_3(OH)_5]$. Precipitation by ferricyanide gives a larger separation factor, but this advantage is nullified by practical difficulties in its operation.

The great relative abundance of yttrium results in initial concentrates of erbium of the order of 10%, and of holmium of 2%. Methods of increasing these to over 50% before application of a final method of purification are here considered. Separation factors have been calculated, and although not constant they do not differ widely for the various basicity processes in nitrate solution which have been most used. When a binary mixture is submitted to a separational process each of the two fractions is enriched in one component. The ratio richer/poorer is the enrichment factor, and the product of the two enrichment factors is the separation factor, as here calculated.

Table 1.* *The basic nitrate–nitrite process.*

	10 g. of nitrate/l. initially (Willard and James)					30 g. of nitrate/l. initially (Wichers, Hopkins, and Balke)						
(*a*)	27·0	26·6	20·2	14·4	11·9	51·7	47·3	39·2	27·1	20·3	11·3	2·2
(*b*)	2·50	2·81	3·39	4·00	12·9	1·98	2·02	2·20	2·36	2·98	2·94	2·00
(*c*)	3·05	3·46	4·00	4·51	14·6	3·03	2·94	2·98	2·86	3·48	3·18	2·02

	2 g. of nitrate/l. initially			25 g. of nitrate/l. initially		
(*d*)	72	66	55	46	30	17
(*e*)	1·32	1·49	1·93	1·66	2·30	2·80
(*f*)	2·16	2·46	3·04	2·23	2·86	3·17

* In all Tables: (*a*) Er_2O_3, %, in enriched fraction after conversion into oxide.
(*b*) Er_2O_3 enrichment factor.
(*c*) Er_2O_3–Y_2O_3 separation factor.
(*d*) Ho_2O_3, %, in enriched fraction after conversion into oxide.
(*e*) Ho_2O_3 enrichment factor.
(*f*) Ho_2O_3–Y_2O_3 separation factor.

The Basic Nitrite–Nitrate Process.—Fogg and James (*J. Amer. Chem. Soc.*, 1922, **44**, 307) found that the basic nitrate $4Y_2O_3.2N_2O_5.17H_2O$ was produced by boiling yttrium nitrate (10 g./l.) with sodium nitrite, but the amount of nitrite in the basic precipitate may be considerable if an excess of sodium nitrite is present in the solution. Data given by Willard and James (*ibid.*, 1916, **38**, 1198) and by Wichers, Hopkins, and Balke (*ibid.*, 1918, **40**, 1615) have been used to determine the yttrium–erbium separation factor. Using solutions containing initially about 2 or 25 g./l. of dissolved oxide, the author has determined values for the yttrium–holmium separation factor (Table 1).

Urea Hydrolysis.—An enrichment factor of 1·36 and a separation factor of 2·36 for 73·8% Er_2O_3 are derivable from data by Fogg and Hess (*ibid.*, 1936, **58**, 1751).

The Crystalline ("4/9ths") Basic Nitrate.—This substance has been formulated as $3Y_2O_3.4N_2O_5.20H_2O$ by James and Pratt (*ibid.*, 1910, **32**, 586), or with $18H_2O$ (Feit, *Z. anorg. Chem.*, 1934, **243**, 276). James and Pratt prepared it by partial decomposition of the nitrate by heat followed by lixiviation, and Feit by solution of oxide in a hot concentrated nitrate solution. This method is to be preferred. The author's results are shown in Table 2.

Table 2. *The 4/9ths nitrate process.*

(*a*)	59	51	41	32	22	2·9	1·2	(*d*) 63	44	36	18
(*b*)	1·18	1·9	2·4	2·9	4·5	2·1	2·1	(*e*) 1·5	2·1	2·2	3·4
(*c*)	2·85	2·83	3·38	3·86	5·45	2·1	2·1	(*f*) 2·35	2·93	2·94	3·95

The Air-borne Ammonia Process.—Since its introduction by F. Trombe (*Compt. rend.*, 1942, **215**, 539) this process has been used by Hilal and Sugden (*J.*, 1949, **135**) and by Hilal (*Z. anorg. Chem.*, 1953, **273**, 241; 1954, **275**, 278) to obtain precipitates from nitrate solutions. These are in general coarsely granular basic nitrates, and not hydroxides as Hilal states, for if dissolved in sulphuric acid they give the brown ring test for nitrates strongly. Some results with holmium material are presented in Table 3.

TABLE 3. *The ammonia gas process.*

(*d*)	63	59	15
(*e*)	1·4	1·8	2·9
(*f*)	2·23	2·98	3·27

The Ferricyanide Precipitation Process.—This has been described previously (*J.*, 1947, 118). The separation factor for erbia is now calculated and values for holmia determined, and the results are presented in Table 4.

TABLE 4. *The ferricyanide precipitation process.*

(*a*)	80	75	67	60	45	(*d*)	57	49	39	27	25	10·6	6·5
(*b*)	1·73	1·86	1·97	2·16	2·64	(*e*)	1·97	2·39	2·47	2·87	4·22	4·10	2·80
(*c*)	4·65	4·46	3·94	3·88	4·00	(*f*)	3·25	3·23	3·46	3·83	4·45	5·45	2·92

The analyses in Tables 1 (*a*), 2 (*a*), and 4 (*a*) were based on apparent atomic-weight determinations; the others are spectrophotometric.

EXPERIMENTAL

The "4/9ths" Basic Nitrate.—This salt is only metastable. It may withstand one recrystallisation but it soon breaks down, and attempts at recrystallisation are unrewarding. The stability and solubility in hot solutions are greater for yttrium than for holmium or erbium, but solubilities in the cold are almost zero.

In carrying out a fractionation by means of this salt, a nitrate solution is prepared of density 1·3—1·35. To this, when just below its boiling point, is added a slurry of oxide, and the whole well stirred till the oxide dissolves. The crystal crop is collected next day. A second crop is obtained by taking a portion of the solution, about 1/8th if rich in erbium, but as much as 1/5th for fairly pure yttrium. This is converted into oxide *via* the oxalate and used as above. The basic salt crops are likely to be contaminated with sulphate at first if the material has previously undergone a separation by double alkali sulphate. The basic nitrate has only a low solubility in hot, very concentrated normal nitrate. The solubility rises with dilution of the nitrate till hydrolysis suddenly sets in, as found by James and Pratt (*J. Amer. Chem. Soc.*, 1910, **32**, 873) to occur also at 25°. The success of the process therefore depends upon control of the concentration to near the density stated, and of the basicity of the solution by limiting the quantity of oxide added. The presence of carbonate or sulphate appears to assist in the breakdown of the crystalline basic salt and so should be avoided. Before addition of oxide, nitrate solutions are rendered distinctly acid and well boiled.

DISCUSSION

As expected, the separation factors for holmium are in all cases below the values for erbium. The ferricyanide precipitation values are larger than for the basic nitrate processes, but no distinct differences can be seen between any of the latter for mixtures of comparable composition. This, it is suggested, is because all are due to the formation of the same basic nitrate which we may term the 1/6th nitrate, and for which the formulation $Y[Y(OH)_5NO_3].2H_2O$ is suggested in the case of the yttrium salt. [Fogg and James's formulation (*loc. cit.*) indicates that four molecules combine with loss of H_2O.] The crystalline, or 4/9ths, basic nitrate, prepared only from concentrated nitrate solutions and unstable in water, is seen to be a double salt of normal nitrate and the 1/6th nitrate:

$$Y(NO_3)_3.5 \text{ or } 6H_2O + Y[Y(OH)_5NO_3].2H_2O \longrightarrow Y(NO_3)_3.Y[Y(OH)_5NO_3].6{\cdot}5 \text{ or } 7{\cdot}5H_2O$$

The low stability of this salt will be understood from the very small loss of water of crystallisation from its constituent simple salts which its formation occasions. It breaks down in insufficiently concentrated nitrate solution, and even in concentrated solution if kept too long especially if hot.

In the cerium group only 1/3rd nitrates are known for lanthanum, cerium, praseodymium, and neodymium (Dutt, *J. Indian Chem. Soc.*, 1945, **22**, 97). The 4/9ths nitrate does not occur earlier in the lanthanon series than samarium, and for this element it is difficult to prepare. Samarium is the point in the series where the pH at incidence of precipitation by alkali is least affected by the lanthanon nitrate concentration (M. Trombe, *Compt. rend.*, 1943, **216**, 888. We may conclude that this Trombe effect is the consequence of the formation in nitrate solution of a somewhat stable and soluble basic nitrate; thus high solubility of the basic nitrate and the large Trombe effect in the case of yttrium are seen to be linked, and likewise the small Trombe effect and the low stability of any basic nitrate of samarium.

Although the separation factor for the ferricyanide precipitation process exceeds those for basic nitrate processes, the labour involved in decomposing the ferricyanide and eliminating iron makes it less advantageous than the 4/9ths basic nitrate process. The latter process makes possible the handling of large amounts of material in small bulk and appears unrivalled for eliminating yttrium from holmium and erbium concentrates.

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, September 16th*, 1954.]

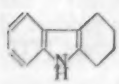
Experiments on the Preparation of Indolocarbazoles. Part VII. Some Derivatives of 5-Amino-1-phenylbenzotriazole.*

By P. H. CARTER, A. R. KATRITZKY, and S. G. P. PLANT.

[Reprint Order No. 5738.]

Some derivatives of 5 : 6 : 7 : 8-tetrahydro-1′-phenyltriazolo(5′ : 4′-3 : 4)-carbazole have been prepared by an extension of Jones and Tomlinson's reaction (*J.*, 1953, 4114) to the appropriate 5-amino-1-phenylbenzotriazoles, and further information has been obtained about this approach to substituted tetrahydrocarbazoles. 5-Amino-1-phenylbenzotriazole has also been converted by other reactions into various substances of quinoline type.

THE reaction by which 1 : 2 : 3 : 4-tetrahydrocarbazole (I) was obtained from aniline and 2-chloro*cyclo*hexanone (D.R.-P. 374,098; *Chem. Zentr.*, 1923, IV, 724) has been used by Campbell and McCall (*J.*, 1950, 2870) for the preparation of a number of simple tetrahydrocarbazoles from the appropriate anilines in yields of 30—60%, but it has given very small yields, if any, of the corresponding product when applied to more complex amines such as the aminotetrahydrocarbazoles and *m*-phenylenediamine (Hall and Plant, *J.*, 1953, 116; Jones and Tomlinson, *ibid.*, p. 4114). It has been found by Jones and Tomlinson (*loc. cit.*) that tetrahydrocarbazoles can be very conveniently obtained, often in good yield, by the somewhat analogous process of heating anilines with 2-hydroxy*cyclo*hexanone and a trace of hydrochloric acid, and they have applied the reaction to the preparation of indolocarbazoles from certain diamines which gave none of the desired product when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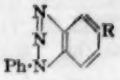
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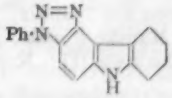
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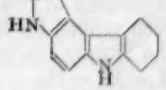
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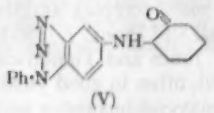
2-chloro*cyclo*hexanone was used. Katritzky and Plant (*J.*, 1953, 412) prepared 5 : 6 : 7 : 8-tetrahydro-1′-phenyltriazolo(5′ : 4′-3 : 4)carbazole (III) from 5-amino-1-phenylbenzotriazole (II; R = NH_2) and 2-chloro*cyclo*hexanone, but further experience has shown that

* Part VI, *J.*, 1953, 412.

the yields are very variable and the product difficult to purify. Coker, Plant, and Turner (*J.*, 1951, 110) have found that the yields of the resulting carbazoles are profoundly affected by substituents in the phenyl group in the application of the Graebe–Ullmann reaction to 5-cyano- (II; R = CN) and 5-nitro-1-phenylbenzotriazoles (II; R = NO_2). It therefore seemed possible that tetrahydroindolo(2′ : 3′-3 : 4)carbazoles of the type (IV) would result from the elimination of nitrogen from derivatives of the compound (III) with substituents in the phenyl group, and that the latter might be conveniently prepared from the correspondingly substituted 5-amino-1-phenylbenzotriazoles and 2-hydroxy-*cyclo*hexanone. Although the ultimate objective was not achieved, the preparation of the required substances (of the type III) has led to useful observations on the Jones and Tomlinson reaction. In its earlier applications the tetrahydrocarbazoles were prepared in a single operation, but the examples now studied have been employed in two stages. The first took place when the reactants were heated together without a catalyst and involved the formation of an intermediate which, although there are possibilities for isomerism, seemed likely to be represented in the case of the parent compound by the structure (V), a view confirmed by its infra-red spectrum. The second stage occurred at a slightly higher temperature in the presence of a catalyst. Concentrated hydrochloric acid was used for this purpose, but was not universally satisfactory, and it was sometimes, but not always, better to replace it by a trace of the dry hydrochloride of the corresponding amine. Attempts to combine the two stages into one operation gave poorer results, and it was an advantage to purify the intermediate. The well-known synthesis of indoles from aromatic amines and 2-halogeno-ketones proceeds through the intermediate 2-anilino-ketones (Crowther, Mann, and Purdie, *J.*, 1943, 58; Brown and Mann, *J.*, 1948, 847, 858; Campbell and McCall, *loc. cit.*), and the close connexion between the reactions is obvious.

During other work, which has been discontinued, the base (II; R = NH_2) and 1-*p*-aminophenylbenzotriazole (VI) have been condensed with ethyl acetoacetate with the formation of the corresponding 4-quinolones through the Conrad–Limpach reaction. The base (II; R = NH_2) has also been converted into 5-acetoacetamido-1-phenylbenzotriazole (II; R = NH·CO·CH_2Ac), but attempts to obtain the corresponding 2-quinolone with sulphuric acid under the conditions ordinarily used for the Knorr reaction (Ewins and King, *J.*, 1913, 103, 104) led to hydrolysis with the formation of the original amine. 5-Acetamido-1-phenylbenzotriazole was similarly hydrolysed. It was possible however to convert the benzotriazole (II; R = NH·CO·CH_2Ac) directly into 2-chloro-4-methyl-1′-phenyltriazolo(4′ : 5′-5 : 6)quinoline (VII; R = Cl; R′ = Me) with phosphorus oxychloride. 5-Chloro-1′-phenyltriazolo(5′ : 4′-3 : 4)acridine (VIII) has been prepared by the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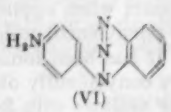
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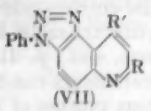
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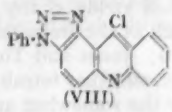
(VIII)

action of phosphorus oxychloride on the product obtained by condensing the base (II; R = NH_2) with *o*-chlorobenzoic acid.

In these various cyclisations with the base (II; R = NH_2) and its derivatives there are two possible structures for the product, but on theoretical grounds and from general experience of related reactions the "linear" form is extremely unlikely. In fact it has been proved by Kulka and Manske (*Canad. J. Chem.*, 1952, 30, 711) that the product of the Skraup reaction with the base (II; R = NH_2) has the "angular" structure (VII; R = R′ = H).

Experimental

Substituted 5-Amino-1-phenylbenzotriazoles.—The amines required for the work described below were prepared by condensation of the appropriate substituted aniline with 1-chloro-2 : 4-dinitrobenzene, reduction with sodium sulphide in hot ethanol to the corresponding derivative of 2-amino-4-nitrodiphenylamine (cf. D.R.-P. 85,388), conversion into the 5-nitro-

1-phenylbenzotriazole (cf. Fries and Empson, *Annalen*, 1912, **389**, 350), and subsequent reduction with zinc dust and aqueous-ethanolic calcium chloride (cf. Beretta, *Gazzetta*, 1925, **55**, 788). The following are new: *5-amino*-1-p-*chlorophenylbenzotriazole* (Blom, *Helv. Chim. Acta*, 1921, **4**, 1036, obtained a crude amine, stated to be unstable, which he converted into the corresponding acetamido-compound without purification), pale brown needles, m. p. 170—171° (from aqueous ethanol) (Found: C, 58·9; H, 3·9. $C_{12}H_9N_4Cl$ requires C, 58·9; H, 3·7%); *2-amino-2'-methoxy-4-nitrodiphenylamine*, orange-red plates, m. p. 146—147° (from carbon tetrachloride) (Found: C, 60·2; H, 4·9. $C_{13}H_{13}O_3N_3$ requires C, 60·2; H, 5·0%); 1-o-*methoxyphenyl-5-nitrobenzotriazole*, needles, m. p. 152—153° (from ethanol) (Found: C, 58·3; H, 3·8. $C_{13}H_{10}O_3N_4$ requires C, 57·8; H, 3·7%); *5-amino*-1-o-*methoxyphenylbenzotriazole*, pale brown rods, m. p. 149° (from aqueous ethanol) (Found: C, 64·5; H, 5·1. $C_{13}H_{12}ON_4$ requires C, 65·0; H, 5·0%); *2-amino-3'-methoxy-4-nitrodiphenylamine*, chocolate-brown needles, m. p. 151—152° (from ethanol) (Found: C, 60·0; H, 5·0%); 1-m-*methoxyphenyl-5-nitrobenzotriazole*, needles, m. p. 201° (from ethanol) (Found: C, 57·8; H, 4·0%); *5-amino*-1-m-*methoxyphenylbenzotriazole*, needles, m. p. 108—109° (from aqueous ethanol) (Found: C, 64·8; H, 5·2%); *5-amino*-1-o-*tolylbenzotriazole*, brown prisms, m. p. 93° (from ethanol) (Found: C, 69·6; H, 5·4. $C_{13}H_{12}N_4$ requires C, 69·6; H, 5·4%). The last-named was converted into *5-acetamido*-1-o-*tolylbenzotriazole*, needles, m. p. 204° (from acetic acid) (Found: C, 67·4; H, 5·5. $C_{15}H_{14}ON_4$ requires C, 67·7; H, 5·3%), by warm acetic anhydride.

5-(2-Oxocyclohexyl)amino-1-phenylbenzotriazole and its Derivatives.—When a mixture of 5-amino-1-phenylbenzotriazole (1 g.) and 2-hydroxy*cyclo*hexanone (0·6 g.) was gradually heated in a paraffin bath, it became completely molten at 126°, and, with continued heating and stirring, solidified at 132° with evolution of water. After the whole had been stirred with hot ethanol, the solid, when cold, was collected and recrystallised from *cyclo*hexanone, from which *5-(2-oxocyclohexyl)amino-1-phenylbenzotriazole* separated in plates (55%), m. p. 169° (Found: C, 70·5; H, 5·8. $C_{18}H_{18}ON_4$ requires C, 70·6; H, 5·9%) [the infra-red spectrum, in Nujol suspension, showed bands at 2·98 μ (>NH) and 5·85 μ (>CO)]. The following were similarly prepared, the temperature reached in the reaction being given in each case in parentheses after the name: 1-p-*chlorophenyl-* (150°), needles (53%), m. p. 200—201° (from *cyclo*hexanone and then ethanol) (Found: C, 63·5; H, 5·1. $C_{18}H_{17}ON_4Cl$ requires C, 63·4; H, 5·0%), 1-o-*methoxyphenyl-* (140°), prisms (55%), m. p. 129—130° [from ethanol (charcoal)] (Found: C, 67·7; H, 6·1. $C_{19}H_{20}O_2N_4$ requires C, 67·9; H, 6·0%), 1-m-*methoxyphenyl-* (145°), plates (46%), m. p. 178° [from ethanol (charcoal)] (Found: C, 68·0; H, 6·0%), and 1-p-*methoxyphenyl-5-(2-oxocyclohexyl)aminobenzotriazole* (145°), needles (45%), m. p. 178—179° [from ethanol (charcoal)] (Found: C, 68·0; H, 6·0%), and *5-(2-oxocyclohexyl)amino*-1-o-*tolylbenzotriazole* (140°), pale brown prisms (51%), m. p. 106—107° [from ethanol (charcoal)] (Found: C, 71·2; H, 6·2. $C_{19}H_{20}ON_4$ requires C, 71·3; H, 6·2%).

5 : 6 : 7 : 8-Tetrahydro-1'-phenyltriazolo(5' : 4' : 3 : 4)carbazole and its Derivatives.—When 5-(2-oxo*cyclo*hexyl)amino-1-phenylbenzotriazole (0·8 g.) was gradually heated with a few drops of concentrated hydrochloric acid, the mixture became molten at 145—150° and solidified again within a few seconds with the evolution of water. After the product had been crystallised from ethanol, 5 : 6 : 7 : 8-tetrahydro-1'-phenyltriazolo(5' : 4'-3 : 4)carbazole was obtained in prisms (0·2 g.), m. p. 221—222°, identical (mixed m. p.) with the substance described by Katritzky and Plant (*loc. cit.*). The following were similarly prepared (the reaction temperature being indicated as before), except that the catalyst in each case was a small amount of the dry hydrochloride of the corresponding amine (prepared by passing dry hydrogen chloride through a suspension of the base in ether): 1'-p-*chlorophenyl-5 : 6 : 7 : 8-tetrahydrotriazolo*(5' : 4'-3 : 4)*carbazole* (180°), prisms (70%), m. p. 251—252° (from ethanol) (Found: C, 66·7; H, 4·9. $C_{18}H_{15}N_4Cl$ requires C, 67·0; H, 4·7%), and *5 : 6 : 7 : 8-tetrahydro*-1'-o-*methoxyphenyl-* (150°), prisms (16%), m. p. 193° [from ethanol (charcoal)] (Found: C, 71·5; H, 6·0. $C_{19}H_{18}ON_4$ requires C, 71·7; H, 5·7%), -1'-m-*methoxyphenyl-* (180°), needles (30%), m. p. 203—204° [from ethanol (charcoal)] (Found: C, 71·4; H, 5·9%), -1'-p-*methoxyphenyl-* (170°), plates (8%), m. p. 245—246° [from ethanol (charcoal)] (Found: C, 71·6; H, 5·8%) (use of concentrated hydrochloric acid as catalyst led to hydrolysis of the 2-oxo*cyclo*hexylamino-group with the isolation of the hydrochloride of 5-amino-1-*p*-methoxyphenylbenzotriazole), and -1'-o-*tolyltriazolo*(5' : 4'-3 : 4)*carbazole* (160°), prisms (53%), m. p. 226—227° [from ethanol (charcoal)] (Found: C, 75·2; H, 6·2. $C_{19}H_{18}N_4$ requires C, 75·5; H, 6·0%).

Although these triazolocarbazoles were heated at different temperatures under various conditions, nothing pure could be isolated from any of the products, except when the conditions were such as to leave unchanged material.

2-Methyl-1'-phenyltriazolo(4' : 5'-5 : 6)quinol-4-one.—After 5-amino-1-phenylbenzotriazole (5 g.), ethyl acetoacetate (5 c.c.), and a few drops of concentrated hydrochloric acid had been left at room temperature for 12 hr. and the solid crystallised from ethanol, *ethyl* β-(*1-phenylbenzotriazol-5-ylamino)crotonate* was obtained in plates (5·5 g.), m. p. 127—128° (Found: C, 67·4; H, 5·8. $C_{18}H_{18}O_2N_4$ requires C, 67·1; H, 5·6%). When the ester (6 g.) was heated for 5 min. at 265°, the product pulverised and extracted with hot benzene, and the residual solid crystallised from nitrobenzene, *2-methyl-1'-phenyltriazolo(4' : 5'-5 : 6)quinol-4-one* was obtained in prisms (2·7 g.), decomp. 325—335° (Found: C, 69·4; H, 4·4. $C_{16}H_{12}ON_4$ requires C, 69·6; H, 4·3%).

The quinolone (1·2 g.), phosphorus oxychloride (10 c.c.), and phosphorus pentachloride (2 g.) were refluxed together for 1½ hr., cooled, and poured into ice and dilute hydrochloric acid. After 1 hr., the solution was filtered and made alkaline with ammonia, and the solid crystallised from aqueous ethanol, to give *4-chloro-2-methyl-1'-phenyltriazolo(4' : 5'-5 : 6)-quinoline* in prisms (0·8 g.), m. p. 183—184° (Found: C, 65·1; H, 3·8. $C_{16}H_{11}N_4Cl$ requires C, 65·2; H, 3·7%).

2-Methyl-6-(benzotriazol-1-yl)quinol-4-one.—Prepared from 1-*p*-aminophenylbenzotriazole as described above for their isomers, *ethyl* β-(p-*benzotriazol-1-ylanilino)crotonate*, first purified by boiling in benzene with charcoal and recovered by evaporation of the filtered solution, was obtained from ethanol in needles (66%), m. p. 130° (Found: C, 67·0; H, 5·7%), and *2-methyl-6-(benzotriazol-1-yl)quinol-4-one* from nitrobenzene in pale brown prisms (45%) which decomposed at 320—340° (Found: C, 69·6; H, 4·4%).

2-Chloro-4-methyl-1'-phenyltriazolo(4' : 5'-5 : 6)quinoline.—When the solid obtained by heating 5-amino-1-phenylbenzotriazole (1·1 g.) with ethyl acetoacetate (0·7 g.) at 180° for 2 min. was crystallised twice from ethanol, *5-acetoacetamido-1-phenylbenzotriazole* was isolated in almost colourless plates (1·2 g.), m. p. 210° (decomp.) (Found: C, 65·0; H, 4·8. $C_{16}H_{14}O_2N_4$ requires C, 65·3; H, 4·8%). After this substance (1·3 g.) had been heated at 100° for 20 min. with concentrated sulphuric acid (25 c.c.), and the whole poured into water, the sulphate (1 g.) of 5-amino-1-phenylbenzotriazole was precipitated. The free base, identified by mixed m. p., was obtained from the salt by adding alkali to its solution in hot water.

5-Acetoacetamido-1-phenylbenzotriazole (2·5 g.) was refluxed with phosphorus oxychloride (12 c.c.) for 4 hr., diluted with chloroform (150 c.c.), and poured into ammonia (150 c.c. of *d* 0·88), and the whole stirred for ½ hr. After the chloroform layer had been dried (Na_2SO_4) and evaporated, the residue was boiled in ethanol with charcoal, and the filtered solution diluted with water. When the precipitate was crystallised first from ethanol and then from light petroleum, *2-chloro-4-methyl-1'-phenyltriazolo(4' : 5'-5 : 6)quinoline* separated in almost colourless prisms (0·2 g.), m. p. 180° (Found: C, 65·3; H, 4·1; Cl, 11·7. $C_{16}H_{11}N_4Cl$ requires Cl, 12·1%).

5-Chloro-1'-phenyltriazolo(5' : 4'-3 : 4)acridine.—5-Amino-1-phenylbenzotriazole (5 g.), *o*-chlorobenzoic acid (3·5 g.), potassium carbonate (4·5 g.), and a little copper bronze were refluxed with amyl alcohol (30 c.c.) for 3 hr., the solvent removed in steam, the residual solution filtered, and the filtrate acidified with acetic acid. The precipitate was dried, refluxed for 2 hr. with phosphorus oxychloride (12 c.c.), and, after the addition of chloroform (150 c.c.), the whole, when cold, was added to a mixture of ice (300 g.) and ammonia (500 c.c. of *d* 0·88). After the mixture had been stirred for ½ hr., the chloroform layer was dried and evaporated. The residual *5-chloro-1'-phenyltriazolo(5' : 4'-3 : 4)acridine* was purified by absorption from benzene on alumina, and it then separated from benzene in prisms (1·5 g.), m. p. 219—221°, which changed above 200° to a polymorphic form, m. p. 229—230° (Found: C, 68·9; H, 3·6. $C_{19}H_{11}N_4Cl$ requires C, 69·0; H, 3·3%).

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2-*Acyl*cyclo*hexane*-1 : 3-*diones. Part II.** 2-*Formyl*-, 2-*Propionyl*-, 2-iso-*Butyryl*-, *and* 2-*Phenylcarbamoyl*-cyclo*hexane*-1 : 3-*dione, and their Conversion into Phenanthridines.*

By N. A. J. Rogers and Herchel Smith.

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Some 2-acyl*cyclo*hexane-1 : 3-diones have been prepared by the action of acid anhydrides and boron trifluoride on *cyclo*hexane-1 : 3-dione; 2-formyl-*cyclo*hexane-1 : 3-dione was obtained by hydrolysis of *N*-2 : 6-dioxo*cyclo*-hexylmethyleneaniline, produced by fusing *cyclo*hexane-1 : 3-dione with *NN'*-diphenylformamidine. 2-Propionyl*cyclo*hexane-1 : 3-dione with aniline gave *N*-2 : 6-dioxo*cyclo*hexylpropylideneaniline which afforded 9-ethyl-5 : 6 : 7 : 8-tetrahydro-8-oxophenanthridine, but 2-*iso*butyryl*cyclo*hexane-1 : 3-dione failed to react. Neither 2 : 6-dioxo*cyclo*hexylmethyleneaniline nor 2-phenylcarbamoyl*cyclo*hexane-1 : 3-dione (prepared from the sodium derivative of *cyclo*hexane-1 : 3-dione and phenyl *iso*cyanate) gave a cyclo-dehydration product.

In Part I * were described the preparation of 2-acetyl*cyclo*hexane-1 : 3-dione (I; R = Me) and its reaction with aniline to give exclusively 1-(2 : 6-dioxo*cyclo*hexyl)ethylidene-aniline (II; R = Me) which afforded a tetrahydromethyloxophenanthridine. This synthesis is a useful modification of Borsche's (*Annalen*, 1910, **377**, 70) and the present work is an attempt to extend it.

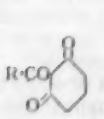
2-Propionyl*cyclo*hexane-1 : 3-dione was first prepared by the method of Part I, from *cyclo*hexane-1 : 3-dione, propionic anhydride, and sodium propionate. The yield was low (13%) and, although improved (to 19%) by use of pyridine as catalyst, indicated that for larger acyl groups other methods of preparation might be preferable. Only 3-acyloxy-*cyclo*hex-2-enones resulted from reaction of acetyl chloride with the sodium derivative of *cyclo*hexane-1 : 3-dione and of the ethoxymagnesium derivative of *cyclo*hexane-1 : 3-dione with acyl chlorides, although the latter method caused *C*-acylations of acetoacetic ester (Viscontini and Merckling, *Helv. Chim. Acta*, 1952, **35**, 2288; Dean, Halewood, Mongkolsuk, Robertson, and Whalley, *J.*, 1953, 1250).

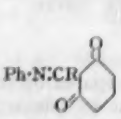
Acylation of *cyclo*hexane-1 : 3-diones with acid anhydrides in the presence of boron trifluoride (Meerwein and Vossen, *J. prakt. Chem.*, 1934, **141**, 149; Dean and Robertson, *J.*, 1953, 1241) had moderate success. Since the dione is insoluble in cold liquid anhydrides the corresponding acids were used as solvents. With this modification the ketones (I; R = Me, Et, and Pr^i) were obtained in yields of 23, 71, and 24% respectively. From these results and those of Meerwein and Vossen (*loc. cit.*) it appears that the yield of triketone is controlled by opposing factors, namely, the size of the entering acyl group and the tendency of the anhydride to condense with itself. Octanoic anhydride (also a liquid at room temperatures) gave only a 2% yield. Benzoic anhydride in chloroform gave a white solid, probably its boron trifluoride complex (cf. Greenwood and Martin, *Quart. Reviews*, 1954, **8**, 1), but no triketone was isolated. Phenylacetic anhydride gave a low yield (8%).

2-Formyl*cyclo*hexane-1 : 3-dione (I; R = H), the first member of the series, was not formed by Claisen condensation of *cyclo*hexane-1 : 3-dione and ethyl formate, probably because *cyclo*hexane-1 : 3-dione is a very strong acid ($K_a \sim 5{\cdot}5 \times 10^{-6}$) (probably stronger than the desired product) and has an unreactive anion. 3-Formyloxy*cyclo*hex-2-enone, which under basic conditions might be rearranged to the *C*-acyl derivative (cf. Wislicenus and Koerler, *Ber.*, 1901, **34**, 218, 3768; Dieckmann and Stein, *Ber.*, 1904, **37**, 3370), could not be prepared by direct or ester-exchange methods. Dains *et al.* (*Ber.*, 1902, **35**, 2496 *et seq.*) showed that *NN'*-diphenylformamidine condenses with compounds containing

* "2-Acetyl*cyclo*hexane-1 : 3-dione," Smith, *J.*, 1953, 803, is regarded as Part I of this series.

reactive methylene groups to give what were described as anilinomethylene derivatives although by prototropy they might equally be methyleneanils. The methyleneanil from *cyclo*hexane-1 : 3-dione was hydrolysed by 2% aqueous sodium carbonate (Mansberg and Shaw, *J.*, 1953, **3467**) to the desired triketone (I; R = H), an unstable oil, which however could be recrystallised at −70°.


(I)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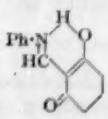
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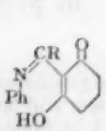
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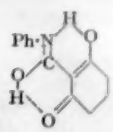
(V)

2-Propionyl*cyclo*hexane-1 : 3-dione and aniline in boiling ethanol gave a good yield of a single anil, which is 1-(2 : 6-dioxo*cyclo*hexyl)propylideneaniline of structure (II; R = Et) since it gives no colour with ferric chloride and is converted by the method of Part I (*loc. cit.*) into 9-ethylphenanthridine (Pictet and Hubert, *Ber.*, 1896, **29**, 1186). 2-*iso*-Butyryl*cyclo*hexane-1 : 3-dione (I; R = Pr^i) could not be induced to react with aniline. The failure of the ring carbonyl groups to react with aniline may be contrasted with the reactivity of both carbonyl groups in 2-acetyl*cyclo*hexan-1-one (Borsche, *loc. cit.*). When in 2-acyl*cyclo*hexane-1 : 3-diones the carbonyl group in the side-chain is sterically hindered, as in (I; R = Pr^i), no reaction with normal carbonyl reagents occurs: protokosin which contains a similar grouping also failed to give carbonyl derivatives (Hems and Todd, *J.*, 1937, 562).

2-Formyl*cyclo*hexane-1 : 3-dione reacted readily with aniline, even in the cold, to give the anil (II; R = H) formed from *NN'*-diphenylformamidine and *cyclo*hexane-1 : 3-dione. This anil, like its analogues (II; R = Me and Et), was soluble in alkali and gave no colour with ferric chloride, but unlike them it gave a copper complex and did not undergo cyclodehydration to a tetrahydro-oxophenanthridine with phosphoric anhydride–phosphoric acid or anhydrous hydrofluoric acid. Failure of the cyclodehydration is typical of anils of β-keto-aldehydes (Claisen and Fischer, *Ber.*, 1888, **21**, 1135; Thielpape, *Ber.*, 1922, **55**, 127; Romet, *Compt. rend.*, 1935, **200**, 1676; Borsche, *loc. cit.*) where it is attributed to the supposed *trans*-configuration about the C=N linkage as compared with the *cis*-configuration thought to be present in the cyclisable anils of β-diketones (Thielpape, *loc. cit.*).

The same explanation may apply to the anil (II; R = H) where complex formation would be favoured by a structure such as (III) and sterically hindered by (IV; R = H) although as Calf and Ritchie (*J. Proc. Roy. Soc. New South Wales*, 1949, **83**, 117) have pointed out, a difference in configuration is not necessarily sufficient to explain the failure of the anils of β-keto-aldehydes to undergo cyclodehydration. Study of the infra-red absorption spectrum of (II; R = H) supports the *trans*-structure since it indicates a chelated carbonyl group (bands at 6·0 and 6·35 μ). The spectra of the anil (II; R = Me) [bands at 6·15 and 6·38 μ (Part I, *loc. cit.*)] and (II; R = Et) (bands at 6·10 and 6·35 μ) are, however, similar in the carbonyl region to those for 2-methyl- and 2-ethyl-*cyclo*hexane-1 : 3-dione [both with bands at 6·10 and 6·35 μ (Part I, *loc. cit.*)] in which chelation is impossible.

Petrow and Hollingsworth (*J.*, 1948, 1537) found that 2'-oxo*cyclo*hexylmethylene-1-naphthylamine was converted into 3 : 4 : 5 : 6-tetrahydro-1-azachrysene by prolonged heating in anhydrous formic acid, supposedly by primary reduction of the C=N bond. By this method the anil (II; R = H), however, gave only a tar, nor was the reduced product formed by magnesium in ethanol (Zechmeister and Truka, *Ber.*, 1930, **63**, 2883) or by hydrogen in the presence of Raney nickel in ethanol. In the last reaction hydrogenolysis to 2-methyl*cyclo*hexane-1 : 3-dione occurred and the analogue (II; R = Me) was similarly converted into 2-ethyl*cyclo*hexane-1 : 3-dione, probably because saturation of the double bond would give a Mannich base and it is known that Mannich bases of phenols are readily hydrogenolysed to alkylphenols (Caldwell and Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 765).

A further attempt to prepare a tetrahydro-1-oxophenanthridine unsubstituted in the 9-position led to an additional triketone. Phenyl *iso*cyanate condenses with compounds containing an active methylene group or their sodium salts to give *C*- rather than *O*-substituted products (Michael, *J. prakt. Chem.*, 1887, **35**, 451; Behrend and Mayer, *Ber.*, 1900, **33**, 623; Dieckmann, *ibid.*, p. 2002; Michael and Cobb, *Annalen*, 1908, **363**, 64; Steinkopf and Daege, *Ber.*, 1911, **44**, 497). The sodium derivative of *cyclo*hexane-1 : 3-dione with phenyl *iso*cyanate in tetrahydrofuran gave 2-phenylcarbamoyl*cyclo*hexane-1 : 3-dione (I; R = NHPh), whose structure follows from its ability to form a copper complex. The triketone decomposed in concentrated sulphuric acid or phosphoric acid–phosphoric anhydride and was recovered unchanged after treatment with anhydrous hydrofluoric acid, although 2-phenylcarbamoyl- (Blount, Perkin, and Plant, *J.*, 1929, 1975) and 2-1′-naphthylcarbamoyl-*cyclo*pentan-1-one (Clemo and Mishra, *J.*, 1953, 192) both cyclise readily to α-quinolones. The ultra-violet absorption spectrum of the carbamoyl compound (I; R = NHPh), unlike that of the 2-acyl*cyclo*hexane-1 : 3-diones, shows no band in the 230—240 mμ region, only an intense band at 270 mμ. This indicates that, in solution at least, it exists as the imidoyl form (V) or a bond isomer which would be stabilised by double chelation, and, containing no αβ-unsaturated ketone grouping, would show no absorption in the 230—240 mμ region (cf. Part I, *loc. cit.*). The intense band at 270 mμ is in accord with the extended system of conjugation present in (V) or its bond isomer.

The anil from the triketone (I; R = Me) and 1-aminonaphthalene was best obtained by Redelien's method (*Annalen*, 1912, **388**, 165). It was cyclised to 3 : 4 : 5 : 6-tetrahydro-2-methyl-3-oxo-1-azachrysene which on reduction and dehydrogenation gave 2-methyl-1-azachrysene (Ritchie, *J. Proc. Soc., N.S.W.*, 1945, **78**, 186). The methyl group in the latter can be replaced by hydrogen (Ritchie, *ibid.*, 1944, **78**, 164; Caldwell, *J.*, 1952, 2035) and so the above synthesis offers a practical route to the 1-azachrysene system which is present in various plant alkaloids.

Experimental

Infra-red spectra were determined for solids as Nujol mulls and for liquids as liquid films. All spectra were determined by Dr. F. B. Strauss with the technical assistance of Mr. F. Hastings.

2-*Propionyl*cyclo*hexane*-1 : 3-*dione* (I; R = Et).—(i) *cyclo*Hexane-1 : 3-dione (35 g.) and anhydrous sodium propionate (6·5 g.) were heated in propionic anhydride (235 g.) at 125° (bath) for 7·5 hr. The anhydride was removed under reduced pressure, the tarry residue was extracted with alkali, and the extracts were acidified. The resulting gum was collected with ether and distilled in steam until the distillate gave no colour with ferric chloride. The distillate was thoroughly extracted with ether, and the extract was washed with water and shaken with an excess of aqueous copper acetate. The copper complex (8·1 g., 13%), m. p. 185° (from chloroform), was filtered off and shaken with 3N-hydrochloric acid (150 c.c.) and ether (200 c.c.). The ethereal solution was washed with water, dried ($MgSO_4$), and evaporated under reduced pressure. Distillation then gave colourless 2-*propionyl*cyclo*hexane*-1 : 3-*dione* (6·3 g.), b. p. 124°/15 mm., m. p. 19° (Found: C, 64·1; H, 7·3. $C_9H_{12}O_3$ requires C, 64·4; H, 7·2%). Light absorption in MeOH: Max. 235 and 275 mμ (ε 9300 and 8300). The infra-red spectrum had bands at 6·00 and 6·40 μ.

(ii) A solution of *cyclo*hexane-1 : 3-dione (5 g.) in propionic acid (20 g.) and propionic anhydride (20 g.) was added dropwise during 1·5 hr. to propionic anhydride (20 g.) and pyridine (2 g.) at the b. p. Refluxing was continued for a further 4·5 hr., then the solvents were removed under reduced pressure. The residue was dissolved in ether, filtered off, washed with water, and shaken with saturated cupric acetate solution. The precipitate was filtered off, dried, and recrystallised from chloroform, to give 2-propionyl*cyclo*hexane-1 : 3-dione copper complex (1·7 g., 19%), m. p. 185°, undepressed by a sample prepared as in (i). Similarly *cyclo*hexane-1 : 3-dione and acetic anhydride gave a 34% yield of 2-acetyl*cyclo*hexane-1 : 3-dione copper complex, m. p. 265°, undepressed on admixture with a sample prepared as described in Part I (*loc. cit.*).

(iii) A solution of *cyclo*hexane-1 : 3-dione (5·2 g.) in propionic anhydride (12·5 g.) and propionic acid (15 g.) was saturated with boron trifluoride (ice-cooling), 17·5 g. being absorbed. Sodium acetate (35 g.) in water (50 c.c.) was added and the mixture distilled in steam until it gave no ferric chloride colour. Working up as under (i) gave 2-propionyl*cyclo*hexane-1 : 3-dione copper complex (6·6 g., 71%), m. p. 185°, undepressed by the sample prepared as in (i). The same method gave a 23% yield of 2-acetyl*cyclo*hexane-1 : 3-dione copper complex, m. p. 265°.

2-iso*Butyryl*cyclo*hexane*-1 : 3-*dione* (I; R = Pr^i).—A solution of *cyclo*hexane-1 : 3-dione (20 g.) in *iso*butyric anhydride (43 g.) and *iso*butyric acid (40 g.) was saturated with boron trifluoride, and the mixture was treated as above. The steam distillate was extracted with ether, and the ethereal solution washed with sodium hydrogen carbonate solution to remove acid, then with water, and was shaken with saturated aqueous cupric acetate. The 2-iso*butyryl*cyclo*hexane*-1 : 3-*dione copper complex* (9·25 g., 24%) had m. p. 228—230° after recrystallisation from aqueous ethanol (Found: C, 56·2; H, 6·4. $C_{20}H_{26}O_8Cu$ requires C, 56·3; H, 6·4%). The complex was decomposed in the usual manner and the product distilled, to give the 2-iso*butyryl*cyclo*hexane*-1 : 3-*dione* (7·25 g.), b. p. 144°/20 mm., m. p. 37—38° (Found: C, 65·9; H, 7·8. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·7%). Light absorption in MeOH: Max. 235 and 275 mμ (ε 14,000 and 13,350). The infra-red spectrum had bands at 6·00 and 6·40 μ.

2-*Octanoyl*cyclo*hexane*-1 : 3-*dione* (I; R = C_7H_{15}).—A solution of *cyclo*hexane-1 : 3-dione (10 g.) in octanoic anhydride (20 g.; cf. Gerrard and Thrush, *J.*, 1952, 741) and octanoic acid (20 g.) was saturated with boron trifluoride. The mixture was treated with sodium acetate (70 g.) in water (100 c.c.), and then distilled in steam to remove most of the acid. The residue was extracted with ether, and the ether washed with sodium hydrogen carbonate solution and water and shaken with saturated aqueous cupric acetate. The green precipitate was filtered off, washed with ether to remove any copper hexanoate, and decomposed in the known manner to an oil, which was dissolved in a little light petroleum (b. p. 40—60°). Chilling at −70° precipitated a buff solid, m. p. 46°, which we did not identify. The residual oil was distilled, to give the 2-*octanoyl*cyclo*hexane*-1 : 3-*dione* (0·26 g.), b. p. 100° (bath-temp.)/0·1 mm. (Found: C, 70·2; H, 9·2. $C_{14}H_{22}O_3$ requires C, 70·6; H, 9·2%). Light absorption in MeOH: Max. 232·5 and 275 mμ (ε = 10,400 and 9900). The infra-red spectrum had bands at 6·00 and 6·45 μ. The *copper complex* prepared from the pure trione had m. p. 132—136° (sealed capillary) after recrystallisation from chloroform–light petroleum (b. p. 60—80°) (Found: C, 62·4; H, 7·7. $C_{28}H_{42}O_6Cu$ requires C, 62·4; H, 7·8%).

2-*Phenylacetyl*cyclo*hexane*-1 : 3-*dione* (I; R = CH_2Ph).—A solution of *cyclo*hexane-1 : 3-dione (1·6 g.) and phenylacetic anhydride (3·5 g., Wedekind, *Ber.*, 1901, **34**, 2070) in chloroform (15 c.c.) was saturated with boron trifluoride. The dark solution was treated with 70% aqueous sodium acetate and extracted with ether. The ethereal solution was washed with sodium hydrogen carbonate solution and water, concentrated, and shaken with saturated aqueous cupric acetate. The copper complex (0·3 g., 8%) had m. p. 182—185° after recrytallisation from chloroform. It was decomposed in the usual manner to yield a solid which separated from light petroleum (b. p. 40—60°) as colourless needles, m. p. 79°, b. p. 175° (bath-temp.)/15 mm. (Found: C, 72·7; H, 6·1. $C_{14}H_{14}O_3$ requires C, 73·1; H, 6·1%). Light absorption in MeOH: Max. 235 and 275 mμ (ε 15,200 and 15,200). The infra-red spectrum had bands at 6·03 and 6·43 μ.

2 : 6-*Dioxo*cyclo*hexylmethyleneaniline* (II; R = H).—A mixture of *cyclo*hexane-1 : 3-dione (15·5 g.) and *NN'*-diphenylformamidine (31 g.) was heated at 130° (bath-temp.) for 1 hr. After cooling, the product was extracted with 5% hydrochloric acid (200 c.c.), washed with water, dried, and recrystallised from light petroleum (b. p. 60—80°) to give 2 : 6-*dioxo*cyclo*hexylmethyleneaniline* as yellow needles (25 g.), m. p. 124—125° (Found: C, 72·2; H, 6·0; N, 6·4. $C_{13}H_{13}O_2N$ requires C, 72·6; H, 6·1; N, 6·5%). The infra-red spectrum had bands at 6·00 and 6·35 μ. The anil was soluble in alkali, reprecipitated on acidification, and soluble in excess of acid. In ether it gave with aqueous cupric acetate a green *copper complex*, m. p. 260—262°, after recrystallisation from chloroform–light petroleum (b. p. 60—80°) (Found: N, 5·2. $C_{26}H_{24}O_4N_2Cu$ requires N, 5·7%). *NN'*-Diphenylacetamidine failed to condense with *cyclo*hexane-1 : 3-dione under the above conditions.

2-*Formyl*cyclo*hexane*-1 : 3-*dione* (I; R = H).—A suspension of the above anil (18 g.) in 2% sodium carbonate solution was boiled in an open vessel, the volume being kept constant by occasional addition of water, until the steam gave no colour with sodium hypochlorite paper. The mixture was then cooled, acidified, saturated with salt, and extracted with ether. The ethereal solution was washed with brine and shaken with saturated aqueous cupric acetate, affording a copper complex which was decomposed in the usual way. The resulting oil was extracted with boiling light petroleum (b. p. 40—60°) until only a resin remained, and the extracts were combined and chilled at −70°. The supernatant liquid was decanted from the mass of colourless crystals, which liquefied on regaining room temperature. The resulting 2-*formyl*cyclo*hexane*-1 : 3-*dione* (8·2 g.) was freed from solvent *in vacuo* (Found: C, 59·7; H, 6·0. $C_7H_8O_3$ requires C, 60·0; H, 5·7%). The triketone resinified when an attempt was made to distil it in bulk, but a small quantity could be distilled with only slight darkening

[b. p. 105° (bath-temp.)/12 mm.]. Light absorption in MeOH : Max. 240 and 255 mμ (ε = 9100 and 9800). The infra-red spectrum had a strong band at 5·98, and a very broad, intense band centred at 6·30 μ. When the trione (1·5 g.) was treated with aniline (1·1 g.) in ethanol (5 c.c.), yellow needles began to separate almost immediately. The reaction was completed by a few minutes' warming on the steam-bath, the mixture was cooled, and the crystals were filtered off. Recrystallisation from light petroleum (b. p. 60—80°) gave the 2 : 6-dioxo*cyclo*hexylmethyleneaniline as needles (1·6 g.), m. p. 124°, undepressed by a sample prepared as described above and possessing an identical infra-red absorption spectrum. Light absorption in MeOH : Max. 235, 255, and 340 mμ (ε 9000, 9600, and 23,700). This spectrum is different from that for the anils [II ; R = Me (Part I, *loc. cit.*) and Et (below)] and is in accord with the *trans*-formulation (III) for the anil. 2-Formyl*cyclo*hexane-1 : 3-dione did not react with *N*-methylaniline in ethanol.

1-(2 : 6-*Dioxo*cyclo*hexyl*)*propylideneaniline* (II ; R = Et).—2-Propionyl*cyclo*hexane-1 : 3-dione (2·5 g.) was refluxed in ethanol (12 c.c.) with aniline (2·0 g.) for 5 hr. The solution was poured into water (100 c.c.). The precipitate, after solidification, was dried and recrystallised from light petroleum (b. p. 60—80°) to give the 1-(2 : 6-*dioxo*cyclo*hexyl*)*propylideneaniline* as colourless needles (2·7 g.), m. p. 74° (Found : C, 74·1 ; H, 7·1 ; N, 6·0. $C_{15}H_{17}O_2N$ requires C, 74·1 ; H, 7·0 ; N, 5·8%). Light absorption in MeOH : Max. 250 and 305 mμ (ε = 17,000 and 19,900). The infra-red spectrum had bands at 6·10 and 6·35 μ.

9-*Ethyl*-5 : 6 : 7 : 8-*tetrahydro*-8-*oxophenanthridine*.—1-(2 : 6-Dioxo*cyclo*hexyl)propylideneaniline (2·5 g.) was heated at 180° with phosphoric anhydride (19 g.) and phosphoric acid (28 g.) for 1 hr. On cooling to 90°, the mixture was poured into water, basified, and extracted with ether, and the ethereal solution washed with water, dried ($MgSO_4$), and evaporated under reduced pressure. The crystalline residue was recrystallised from light petroleum to give the 9-*ethyl*-5 : 6 : 7 : 8-*tetrahydro*-8-*oxophenanthridine* as buff needles (1·5 g.), m. p. 77° (Found : C, 80·0 ; H, 6·6 ; N, 6·2. $C_{15}H_{15}ON$ requires C, 80·0 ; H, 6·7 ; N, 6·2%). Light absorption in MeOH : Max. 240, 285, and 325 mμ (ε = 28,600, 8300, and 1300). The infra-red spectrum had a band at 5·95 μ.

9-*Ethyl*-5 : 6 : 7 : 8-*tetrahydro*-8-*hydroxyphenanthridine*.—The above ethyltetrahydro-oxophenanthridine (0·8 g.) in dry ether (60 c.c.) was refluxed with lithium aluminium hydride (0·3 g.) in ether (80 c.c.) for 30 min. 9-*Ethyl*-5 : 6 : 7 : 8-*tetrahydro*-8-*hydroxyphenanthridine* was obtained from ethyl acetate–light petroleum (b. p. 60—80°) as needles (0·20 g.), m. p. 114° (Found : N, 5·8. $C_{15}H_{17}ON$ requires N, 6·1%). Light absorption in MeOH : Max. 235, 275, 305, and 320 mμ (ε 25,600, 5300, 4200, and 3200). The infra-red spectrum had bands at 2·80, 3·05, and 3·25 μ.

9-*Ethylphenanthridine*.—The preceding compound (130 mg.) was heated with 30% palladised charcoal (20 mg.) at 260° for 25 min. The dark residue was extracted with warm ether (4 × 20 c.c.) and boiling ethanol (20 c.c.), and the extracts were combined, dried, and evaporated to a gum which was extracted with boiling light petroleum (b. p. 60—80° ; 4 × 20 c.c.). The product was passed in light petroleum (b. p. 40—60°) through activated alumina (5 g.). The resulting oil crystallised and gave 9-ethylphenanthridine as colourless needles (40 mg.), m. p. 55·5°, from light petroleum (b. p. 40—60°) (Found : C, 86·6 ; H, 6·4 ; N, 6·7. Calc. for $C_{15}H_{13}N$: C, 87·0 ; H, 6·3 ; N, 6·8%). Light absorption in MeOH : Max. 250, 300, 345, and 365 mμ (ε 33,100, 5700, 4100, and 4100). Pictet and Hubert (*loc. cit.*) give 54—55°.

2-*Methyl*cyclo*hexane*-1 : 3-*dione*.—2 : 6-Dioxo*cyclo*hexylmethyleneaniline (1 g.) in ethanol (30 c.c.) containing freshly prepared Raney nickel was shaken with hydrogen until 1 mol. had been absorbed. The catalyst was filtered off, the filtrate evaporated under reduced pressure, and the residue washed with a little dry benzene. The product, recrystallised from benzene, gave 2-methyl*cyclo*hexane-1 : 3-dione (0·20 g.), m. p. and mixed m. p. 206°, possessing the authentic infra-red absorption spectrum. The benzene washings were evaporated to a gum which was extracted with boiling light petroleum (b. p. 60—80°). The extracts deposited unchanged 2 : 6-dioxo*cyclo*hexylmethyleneaniline, m. p. 122°.

2-*Ethyl*cyclo*hexane*-1 : 3-*dione*.—1-(2 : 6-Dioxo*cyclo*hexyl)ethylideneaniline (0·5 g.) was hydrogenated at 1 atm. in ethanol (25 c.c.) over Raney nickel until 2 mols. had been absorbed (12 hr.). 2-Ethyl*cyclo*hexane-1 : 3-dione was obtained from benzene as leaflets (0·15 g.), m. p. 176° (Found : C, 68·7 ; H, 8·5. Calc. for $C_8H_{12}O_2$: C, 68·6 ; H, 8·6%).

2-*Phenylcarbamoyl*cyclo*hexane*-1 : 3-*dione* (I ; R = NHPh).—*cyclo*Hexane-1 : 3-dione (3 g.) in methanol (20 c.c.) was added to sodium methoxide (from the metal, 0·55 g.) in methanol, and the solution evaporated to dryness under reduced pressure. The resulting sodium salt was finely powdered by shaking, and refluxed in suspension, in pure tetrahydrofuran (40 c.c.)

with phenyl *iso*cyanate (3 g.) for 3 hr. The solvent was removed under reduced pressure and the residue decomposed with dilute acid. The mixture was extracted with ether, and the ethereal solution washed with water and shaken with saturated aqueous cupric acetate. The 2-*phenylcarbamoyl*cyclo*hexane*-1 : 3-*dione copper complex* (5·1 g.), m. p. 277° (decomp.), was insoluble in chloroform (Found : N, 5·3. $C_{26}H_{24}O_6N_2Cu$ requires N, 5·3%). It was decomposed in the usual way to give 2-*phenylcarbamoyl*cyclo*hexane*-1 : 3-*dione* separating from ethanol as buff prisms (4·1 g.), m. p. 77° (Found : C, 67·5; H, 6·0; N, 6·0. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·7; N, 6·0%). Light absorption (methanol) : Max. 270 mμ (ε 20,600). The infra-red spectrum had bands at 6·06, 6·30, and 6·48 μ. The product was soluble in alkali and gave a blood-red colour with ferric chloride.

1′-(2 : 6-*Dioxo*cyclo*hexyl*)*ethylidene*-1-*naphthylamine*.—(i) 2-Acetyl*cyclo*hexane-1 : 3-dione (1·53 g.) and 1-naphthylamine (1·55 g.) were refluxed in ethanol (10 c.c.) for 6 hr. When cold, the solution was poured into water and the precipitate was filtered off, dried, and recystallised from ethyl acetate–light petroleum (b. p. 60—80°) to give the *anil* as needles (1·35 g.), m. p. 144—145° (Found : C, 77·1; H, 6·2; N, 5·3. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·1; N, 5·0%). Light absorption in MeOH : Max. 225, 250, and 310 mμ (ε 28,700, 16,600, and 18,900). The anil was soluble in alkali and gave no colour with aqueous-ethanolic ferric chloride.

(ii) 1-Naphthylamine–zinc chloride complex (0·1 g.), prepared by grinding powdered zinc chloride (1 mol.) with 1-naphthylamine (2 mols.) on the steam-bath, was added to acetyl*cyclo*hexane-1 : 3-dione (1·25 g.) and 1-naphthylamine (1·1 g.) at 150°, vigorous evolution of steam occurring. The temperature was raised to 180° during 30 min. and the mixture, on cooling, was extracted with chloroform. The combined extracts were filtered. The product was recrystallised from ethanol to give the above anil (1·6 g.), m. p. 144—145°.

3 : 4 : 5 : 6-*Tetrahydro*-2-*methyl*-3-*oxo*-1-*azachrysene*.—The above anil (1·2 g.) was cyclised in the usual way with phosphoric anhydride (9·5 g.) and phosphoric acid (8 c.c.) at 170°. 3 : 4 : 5 : 6-*Tetrahydro*-2-*methyl*-3-*oxo*-1-*azachrysene*, from ethyl acetate–light petroleum (b. p. 60—80°), formed buff needles (0·75 g.), m. p. 154° (Found : C, 82·8; H, 5·8; N, 5·4. $C_{18}H_{15}ON$ requires C, 82·5; H, 5·8; N, 5·4%). Light absorption in MeOH : Max. 235, 270, 295, 350, and 370 mμ (ε = 8800, 34,000, 12,400, 1700, and 1700).

3 : 4 : 5 : 6-*Tetrahydro*-3-*hydroxy*-2-*methyl*-1-*azachrysene*.—The preceding base (0·605 g.) was reduced with sodium borohydride (0·25 g.) in boiling methanol (70 c.c.) for 20 min. Excess of borohydride was decomposed by dilute acetic acid, the solution was then basified and extracted with ether (4 × 30 c.c.). The ethereal solution was washed with brine, dried, and evaporated under reduced pressure. 3 : 4 : 5 : 6-*Tetrahydro*-3-*hydroxy*-2-*methyl*-1-*azachrysene* formed prisms (0·40 g.), m. p. 155—156°, from ethyl acetate (Found : C, 82·1; H, 6·5; N, 5·3. $C_{18}H_{17}ON$ requires C, 81·6; H, 6·3; N, 5·7%). Light absorption in MeOH : Max. 245, 270, 300, 317·5, 333, and 350 mμ (ε = 25,700, 27,000, 9250, 2000, 3500, and 3600).

2-*Methyl*-1-*azachrysene*.—The tetrahydro-compound (141 mg.) was heated with 30% palladised charcoal (24 mg.) at 260° for 25 min. The residue was extracted with boiling ethanol (25 c.c.) and ether (4 × 20 c.c.). The extracts were combined, dried, and evaporated under reduced pressure to a gum. Chromatography in light petroleum (b. p. 60—80°) on alumina gave 2-*methyl*-1-*azachrysene* obtained from the same solvent as irregular prisms (40 mg.), m. p. 115—116° (Ritchie, *J. Proc. Roy. Soc., N.S.W.*, 1945, **78**, 186, gives m. p. 117°) (Found : C, 88·7; H, 5·4; N, 5·4. Calc. for $C_{18}H_{13}N$: C, 88·9; H, 5·4; N, 5·8%). Light absorption in MeOH : Max. 225, 310, and 360 mμ (ε = 23,100, 5000, and 3000).

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The Resistance of Bact. lactis aerogenes (Aerobacter aerogenes) *to* 8-*Hydroxyquinoline.*

By D. E. F. Hughes and Sir Cyril Hinshelwood.

[Reprint Order No. 5744.]

Cultures of *Bact. lactis aerogenes* can be adapted, by growth in media containing 8-hydroxyquinoline in progressively increased concentrations, to yield resistant strains. The resistance is graded to the maximum concentration in previous exposures. The catalase activity of adapted strains appears to be lower than normal.

The response of *Bact. lactis aerogenes* (*Aerobacter aerogenes*) to toxic or antibacterial agents varies, as with other organisms, both in type and in degree. Forms resistant to phenol develop with extreme difficulty if at all, while " training," for example, to sulphonamides, occurs with comparative ease. This means that the study of any new example possesses a certain interest of its own, which is increased by another factor, namely, the relation between the quantitative degree of the response and the concentration of the agent to which the bacteria have been exposed. In their simplest form adaptation theories of drug resistance involve a graded relation between the resistance of the trained strains and the concentration of the drug to which the cells have been subjected, while in its simplest form the theory of the selection of independent resistant mutants would predict the emergence of a few specific resistant types not closely defined by the exposure. Modifications of either theory provide for a more complex picture. Nevertheless the characteristic relation between " training concentration " and response remains of interest in each separate case.

The present work deals with 8-hydroxyquinoline which further possesses one specific point of interest. If this well-known chelating agent acted by blocking essential and irreplaceable trace metals in the cell, no adaptation would presumably be possible, though metallic antagonists could be found. In fact, however, well-marked and continuously graded resistance develops with comparative ease.

Experimental

Experimental Methods.—The organism was that used by Phillips and Hinshelwood (*J.*, 1953, 3679), and the media were the same except that the iron content was more exactly defined, 0·2 mg./l. of added ferrous sulphate being present. Other heavy metals were confined to those present in " AnalaR " reagents, or in water doubly distilled from all-glass apparatus.

The criterion of resistance is the absence of lag in the growth of cells transferred from a dividing culture to a fresh supply of medium containing the 8-hydroxyquinoline. With a culture not previously exposed the lag rises from zero in a drug-free medium towards infinity with about 10 mg./l. as shown in the left-hand curve of the Figure.

The " training " procedure consisted in serial culture in media containing a fixed amount of the 8-hydroxyquinoline until no further improvement took place. The relation between the lag of the resulting strain and the concentration of the drug in a series of test media was then determined. The strain trained to this first stage was then given a further series of culturings at a given greater concentration, and so on. Lag–concentration curves were determined for each stage of training as shown in the Figure.

Results and Discussion

The lag–concentration curve of the original strain is the left-hand curve. The generation times (time required in logarithmic growth for number of cells to double) are given in Table 1. The generation times rise much less steeply than the lags, but this has little

Table 1. *Concentration of* 8-*hydroxyquinoline and generation time.*

Concn. (mg./l.)	0	1	3	4	5	6	8	10
Gen. time (min.)	32	34	35	43	47	41	41	49

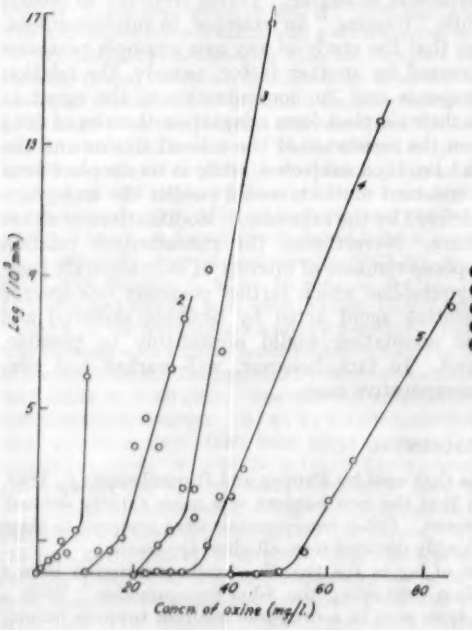
significance : the measurements cannot, from their nature, be made until growth has begun and by this time adaptation (or selection) is already under way.

The resistant strains do not emerge at once (as they would if pre-existent single-step mutants were selected). This is indicated in Table 2. A lag of 50 min. being of little significance, the last strain referred to in Table 2 was used for the training to 20 mg./l. It

TABLE 2.

No. of subcultures at 10 mg./l.	1	2	11
Lag in test at this concn. (min.)	6000	1900	50

was tested after 16 and 31 culturings at this higher concentrations with results shown by the appropriate curves in the Figure. It will be seen that the resistance continues to



Curve 1, Untrained strain.
Curve 2, Strain given 11 subcultures at 10 mg./l.
Curve 3, " 16 " 20 mg./l.
Curve 4, " 31 " 20 mg./l.
Curve 5, " 16 " 40 mg./l.

increase over a considerable number of subcultures (each of which in the conditions of growth involves about 8 successive cell divisions).

The right-hand curve shows the behaviour of the strain which had received 16 subcultures at 40 mg./l.

The curves are spaced out in a way which shows a more or less continuously graded response. No single parameter will adequately express their displacement since they become progressively less steep as they are displaced to the right. The most important characteristic, however, is the point at which the very rapid increase of lag sets in. For an approximate measure of this we may take the concentration at which the lag reaches a standard value of 1000 minutes. On this basis Table 3 may be constructed. There is a distinct parallelism between the numbers in the top row and those in the bottom. The latter increase rather more rapidly. This, combined with the progressive flattening of the curves, suggests a tendency for cells sufficiently trained to reach a state where no concentration of the 8-hydroxyquinoline has any further effect. Reasons for such behaviour have been discussed elsewhere (Peacocke and Hinshelwood, *J.*, 1948, 2290). Nevertheless over

a wide range the resistance developed is closely governed by the maximum concentration to which the cells have been exposed. This behaviour is characteristic either of a physiological adaptation, or of a complex series of mutations each attended with a small increase only in the resistance. It is not proposed to debate here these two alternatives.

TABLE 3. *Family of lag–concentration curves (units are mg./l.).*

Concn. of previous exposures	0	10	20	40
Concn. in test at which lag is 1000 min.	7	17	36	56
Increment caused by training	0	10	29	49

The main interest of the result is that whatever part of the cell mechanism the 8-hydroxyquinoline inactivates, or whatever growth requisite it removes, the interference can be compensated for.

With the idea that the 8-hydroxyquinoline might have a strong action on the iron-containing catalase of the cells, and that there might be significant changes in the readiness of the adapted cells to form this enzyme, experiments were made on its production during the growth cycle of trained and of untrained cells. The method of study was that used by Cole and Hinshelwood (*Trans. Faraday Soc.*, 1946, **43**, 266). Cells which had become adapted to 20 mg. of 8-hydroxyquinoline per l. were found to form less catalase at any stage of the growth cycle, but the formation began earlier and reached its maximum sooner than with the original unadapted strain. No detailed explanation of this is offered at the moment.

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The Synthesis and Reactions of Branched-chain Hydrocarbons. Part VI. The Free-radical Dimerisation of Some Esters and Ketones.*

By M. F. ANSELL, W. J. HICKINBOTTOM, and P. G. HOLTON.

[Reprint Order No. 5762.]

A modified procedure for the preparation and use of acetyl peroxide is described and applied to the dimerisation of ethyl *iso*butyrate, methyl αββ-trimethylbutyrate, 3-methylbutan-2-one, 2 : 5-dimethylpentan-3-one, and 2 : 2 : 4-trimethylpentan-3-one. The resulting diones or diesters have been reduced to the corresponding diols.

THE discovery by Kharasch *et al.* (*J. Org. Chem.*, 1945, **10**, 386, 394, 401) that the decomposition of acetyl peroxide dissolved in aliphatic acids, esters, or ketones, containing a tertiary α-hydrogen atom (I or III), readily yields compounds containing two or more quaternary carbon atoms (II or IV) offers a route to compounds which are otherwise not readily accessible. A disadvantage of this procedure is the hazard involved in handling acetyl peroxide. We have found, however, that by adapting to our own needs the procedure of Rudolf and McEwen (U.S.P. 2,458,207) acetyl peroxide may be prepared in solution in the compound to be dimerised, thereby minimising the danger of explosion.

$R{\cdot}CO{\cdot}CHMe_2$	$(R{\cdot}CO{\cdot}CMe_2{-})_2$	$R{\cdot}CHMe{\cdot}CO_2R'$	$(R{\cdot}\overset{|}{C}Me{\cdot}CO_2R')_2$
(I)	(II)	(III)	(IV)

By this method, the ketones (I), in which R = Me, Pr^i, and Bu^t, and the esters (III), in which (*a*) R = Me, R′ = Et, and (*b*) R = Bu^t, R′ = Me, have been dimerised. The diones or diesters produced have been reduced with lithium aluminium hydride to the corresponding diols.

* Part V, *J.*, 1954, 4197.

Experimental

Ethyl Tetramethylsuccinate (IV; R = Me, R′ = Et).—To a well-stirred mixture of ethyl *iso*butyrate (93 g.), acetic anhydride (130·7 g.), and hydrogen peroxide (100-vol.; 77·5 g.), cooled to 0° in ice–salt was added 23% sodium carbonate solution at such a rate that the temperature did not exceed 55°. Addition was continued until the mixture had pH 6. When the mixture had cooled to 10°, the organic layer was separated, dried (Na_2SO_4; 1½ hr.), and filtered, and the filter was washed with ethyl *iso*butyrate. The resulting solution of acetyl peroxide was added during 2½ hr. to well-stirred boiling ethyl *iso*butyrate (97 g.). After further heating and stirring (2½ hr.) the mixture was cooled, washed with 5% sodium carbonate solution, and dried ($CaCl_2$). Distillation at atmosphere pressure gave methyl acetate (1·2 g.), b. p. 55—60°, and ethyl *iso*butyrate (116 g.), b. p. 109·5—111°. The residue was distilled under reduced pressure to yield ethyl tetramethylsuccinate (37·9 g.), b. p. 124—127°/20 mm., n_D^{20} 1·4349—1·4360. A redistilled portion had b. p. 125—127°/20 mm., n_D^{20} 1·4359 (Hudson and Hauser, *J. Amer. Chem. Soc.*, **1941**, **63**, 3161, record b. p. 119—121°/15 mm.). Hydrolysis with concentrated sulphuric acid gave tetramethylsuccinic anhydride, m. p. 145—145·5°, which was converted into tetramethylsuccinic acid, m. p. 192° (Hudson and Hauser, *loc. cit.*, record m. p. 147° and 194—196° respectively).

2 : 2 : 3 : 3-*Tetramethylbutane*-1 : 4-*diol*.—A solution of ethyl tetramethylsuccinate (26 g.) in dry ether (50 c.c.) was added dropwise to a well-stirred suspension of lithium aluminium hydride (10 g.) in ether (250 c.c.). The mixture was heated under reflux for 1 hr., then cooled, and water (80 c.c.) slowly added, followed by sufficient 5N-sulphuric acid to remove the aluminium hydroxide. The ethereal layer was separated and the aqueous layer extracted with ether (4 × 30 c.c.). Evaporation of the dried (Na_2SO_4) combined extracts left a solid which on crystallisation from light petroleum (b. p. 60—80°) gave pure 2 : 2 : 3 : 3-*tetramethylbutan*-1 : 4-*diol* (14·2 g.), m. p. 224° (Found: C, 65·6; H, 12·1. $C_8H_{18}O_2$ requires C, 65·7; H, 12·4%). The *bis*-3 : 5-*dinitrobenzoate* was insoluble in most solvents; when washed with ether it had m. p. 186° (Found: C, 49·3; H, 4·0; N, 10·3. $C_{22}H_{22}O_{12}N_4$ requires C, 49·4; H, 4·1; N, 10·5%). The *ditoluene*-p-*sulphonate*, m. p. 109°, formed plates from benzene–light petroleum (Found: C, 58·1; H, 6·8; S, 14·5. $C_{22}H_{30}O_6S_2$ requires C, 58·1; H, 6·7; S, 14·1%). Oxidation of the diol with alkaline permanganate gave tetramethylsuccinic acid, m. p. and mixed m. p. 192°.

3 : 3 : 4 : 4-*Tetramethylhexane*-2 : 5-*dione* (II; R = Me).—A solution of acetyl peroxide in 3-methylbutan-2-one (250 g.), prepared as above from acetic anhydride (260 g.), hydrogen peroxide (100-vol.; 160 g.), and 23% sodium carbonate solution, was added dropwise (4 hr.) to boiling 3-methylbutan-2-one (190 g.). After further heating and stirring (2 hr.) the mixture was cooled, washed with 5% sodium carbonate solution, dried (Na_2SO_4) and distilled at atmospheric pressure to give methyl acetate (2·3 g.), b. p. 55—60°, and 3-methylbutan-2-one (355 g.). The residue was distilled under reduced pressure to yield after a small fore-run 3 : 3 : 4 : 4-tetramethylhexane-2 : 5-dione (47·5 g.), b. p. 108—115°/22 mm., n_D^{20} 1·4539—1·4541 (Kharasch, McBay, and Urry, *J. Amer. Chem. Soc.*, 1948, **70**, 1269, record b. p. 40°/0·5 mm., n_D^{20} 1·4522). The *disemicarbazone*, m. p. 222° (decomp.), was insoluble in most solvents; it was washed with ether (Found: C, 47·3; H, 8·1; N, 26·8. $C_{12}H_{24}O_2N_6,H_2O$ requires C, 47·7; H, 8·7; N, 27·8%). The *bis*-2 : 4-*dinitrophenylhydrazone*, m. p. 192°, formed orange-red crystals from alcohol (Found: C, 50·0; H, 5·1; N, 20·8. $C_{22}H_{26}O_8N_8$ requires C, 49·8; H, 4·9; N, 20·7%), and the tetrabromo-derivative, m. p. 116—117°, white needles from alcohol (Kharasch, McBay, and Urry, *loc. cit.*, record m. p. 117°). Oxidation of the diketone with 50% nitric acid gave tetramethylsuccinic acid, m. p. and mixed m. p. 190—192°.

3 : 3 : 4 : 4-*Tetramethylhexane*-2 : 5-*diol*.—The above diketone (56·9 g.) was reduced as for ethyl tetramethylsuccinate, using lithium aluminium hydride (7 g.), to yield the *diol*, m. p. 71—72° (from light petroleum) (Found: C, 68·9; H, 12·7. $C_{10}H_{22}O_2$ requires C, 68·9; H, 12·7%). Its *bis*-3 : 5-*dinitrobenzoate* had m. p. 171° (from benzene–light petroleum) (Found: C, 51·1; H, 4·8; N, 9·6. $C_{24}H_{26}O_{12}N_4$ requires C, 51·2; H, 4·7; N, 10·0%). The glycol could not be distilled as it decomposed to 2 : 3 : 3 : 4 : 4 : 4-*hexamethyltetrahydrofuran*, b. p. 99·5—100·5°/17 mm., n_D^{20} 1·4424 (Found: C, 76·9; H, 12·8. $C_{10}H_{20}O$ requires C, 76·9; H, 12·9%).

2 : 4 : 4 : 5 : 5 : 7-*Hexamethyloctane*-3 : 6-*dione* (II; R = Pr^i).—A solution of acetyl peroxide in 2 : 4-dimethylpentan-3-one (356 g.) prepared as above from acetic anhydride (390 g.), hydrogen peroxide (100-vol.; 240 g.), and 23% sodium carbonate solution was added dropwise (4 hr.) to boiling 2 : 4-dimethylpentan-3-one (320 g.). After further heating (2 hr.), working

up as in the preceding case gave methyl acetate (2·8 g.), b. p. 56—58°, 2 : 4-dimethylpentan-3-one (5·63 g.), and 2 : 4 : 4 : 5 : 5 : 7-hexamethyloctane-3 : 6-dione (40 g.), b. p. 108—114°/5·5 mm., n_D^{20} 1·4520—1·4526. Redistillation gave a pure sample, b. p. 108—111·5°/5·5 mm., n_D^{20} 1·4525 (Kharasch, McBay, and Urry, *loc. cit.*, record b. p. 75—77°/1·5 mm., n_D^{20} 1·4520). No carbonyl derivatives could be formed. Oxidation with 60% nitric acid gave tetramethylsuccinic acid, m. p. and mixed m. p. 190°.

2 : 4 : 4 : 5 : 5 : 7-*Hexamethyloctane*-3 : 6-*diol*.—The above diketone (12·2 g) was reduced with lithium aluminium hydride (2 g.) as for ethyl tetramethylsuccinate, to yield the *diol* (7·1 g.) as a viscous liquid, b. p. 119—121°/3·5 mm., which after four months had deposited cubic crystals, m. p. 84° (Found : C, 73·2; H, 13·0. $C_{14}H_{30}O_2$ requires C, 73·0; H, 13·1%). The diol failed to yield any derivatives.

2 : 2 : 4 : 4 : 5 : 5 : 7 : 7-*Octamethyloctane*-3 : 6-*dione* (II; R = Bu^t).—A solution of acetyl peroxide in 2 : 2 : 4-trimethylpentan-3-one (260 g.), prepared from acetic anhydride (260 g.), hydrogen peroxide (100-vol.; 160 g.), and 23% sodium carbonate solution, was added dropwise (6 hr.) to boiling 2 : 2 : 4-trimethylpentan-3-one (80 g.). After further boiling (1 hr.) the mixture was washed with 5% sodium carbonate solution and dried ($MgSO_4$). Distillation gave 2 : 2 : 4-trimethylpentan-3-one (265 g.), b. p. 71—73°/93 mm., followed, after a small intermediate fraction, by 2 : 2 : 4 : 4 : 5 : 5 : 7 : 7-*octamethyloctane*-3 : 6-*dione* (9·0 g.), a viscous liquid, b. p. 108—115°/1 mm., n_D^{20} 1·4572—1·4581. Redistillation gave a pure sample, b. p. 118—122°/1·5 mm., n_D^{20} 1·4581 (Found : C, 75·4; H, 11·8. $C_{16}H_{30}O_2$ requires C, 75·5; H, 11·9%). No carbonyl derivatives could be prepared. Oxidation with 60% nitric acid gave tetramethylsuccinic acid, m. p. and mixed m. p. 192°.

2 : 2 : 4 : 4 : 5 : 5 : 7 : 7-*Octamethyloctane*-3 : 6-*diol*.—The above diketone (11·3 g.) was reduced as above to the *diol* (8·1 g.), a viscous liquid, b. p. 123—128°/3·5 mm., n_D^{20} 1·4750—1·4766. Redistillation gave a pure sample, b. p. 126—128°/3·5 mm., n_D^{20} 1·4765 (Found : C, 74·3; H, 13·0. $C_{16}H_{34}O_2$ requires C, 74·4; H, 13·3%). No derivatives could be obtained.

Dimethyl 2 : 2 : 3 : 4 : 5 : 5-*Hexamethylhexane*-3 : 4-*dicarboxylate* (IV; R = Bu^t, R′ = Me).—A solution of acetyl peroxide in methyl αββ-trimethylbutyrate (300 g.) (Aston, Clarke, Burgess, and Greenberg, *J. Amer. Chem. Soc.*, 1942, **64**, 300) prepared as above from acetic anhydride (360 g.), hydrogen peroxide (100-vol.; 220 g.), and 23% sodium carbonate solution, was added dropwise (4 hr.) with stirring to methyl αββ-trimethylbutyrate (240 g.) at 100°. After further heating and stirring (2 hr.) the mixture was cooled, washed with 5% sodium hydroxide solution, and water, dried ($CaCl_2$), and distilled to remove unchanged methyl αββ-trimethylbutyrate (409·6 g.), b. p. 89—92°/12 mm. The residue was combined with that obtained from another preparation (406 g. ester used; 286·7 g. recovered) and distilled to yield *dimethyl* 2 : 2 : 3 : 4 : 5 : 5-*hexamethylhexane*-3 : 4-*dicarboxylate* (59·1 g.), b. p. 118—127°/5 mm., n_D^{20} 1·4597—1·4604. A redistilled sample had b. p. 124—126°/5 mm., n_D^{20} 1·4602 (Found : C, 67·4; H, 10·9. $C_{16}H_{30}O_4$ requires C, 67·1; H, 10·6%). The ester could not be hydrolysed on boiling with either sulphuric acid or a solution of potassium hydroxide in diethylene glycol.

2 : 3-*Di*-tert.-*butyl*-2 : 3-*dimethylbutane*-1 : 4-*diol* (3 : 4-*Bishydroxymethyl*-2 : 2 : 3 : 4 : 5 : 5-*hexamethylhexane*).—The above ester (20 g.) was reduced with lithium aluminium hydride (3·5 g.) as for ethyl tetramethylsuccinate to give the *diol* (10·6 g.), a viscous oil, b. p. 123—124°/3·5 mm., n_D^{20} 1·4739 (Found : C, 73·4; H, 12·7. $C_{14}H_{30}O_2$ requires C, 73·0; H, 13·1%), giving, with difficulty, a *bis*-3 : 5-*dinitrobenzoate*, m. p. 242°, needles from benzene (Found : C, 54·0; H, 5·8; N, 9·4. $C_{28}H_{34}O_{12}N_4$ requires C, 54·4; H, 5·5; N, 9·1%).

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Absorption Spectra of Ketones. Part II. The Configuration of Some Bromo-derivatives of 6-Oxocholestanyl Acetate. Absorption Spectra of α-Ketols.*

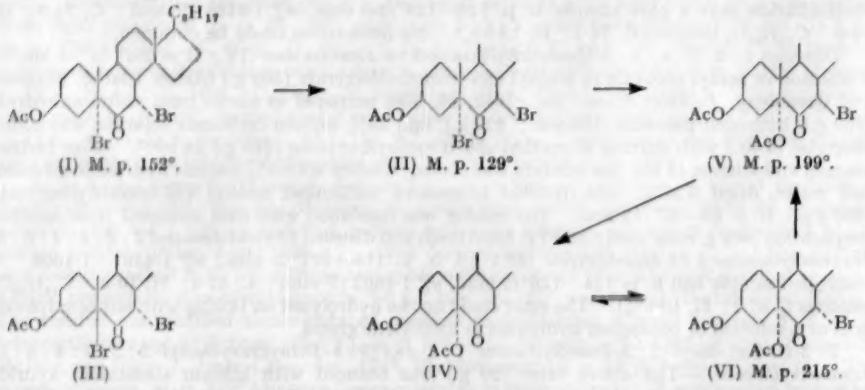
By R. C. Cookson and S. H. Dandegaonker.

[Reprint Order No. 5769.]

3β : 5α-Diacetoxy-7β-bromocholestan-6-one results from acetolysis of 3β-acetoxy-5α : 7β-dibromocholestan-6-one, and the 7α-epimer from bromination of 3β : 5α-diacetoxycholestan-6-one.

The shift of the absorption band of a *cyclo*hexanone caused by substitution of an α-hydroxy- or α-acetoxy-group in an equatorial or an axial configuration parallels the shift produced by an α-bromine atom. Hydroxyl has a greater effect than acetoxyl.

In a thorough investigation of the bromination of 3β-acetoxycholestan-6-one Heilbron, Jackson, Jones, and Spring (*J.*, **1938**, 102) found that the first product of dibromination in acetic acid containing hydrogen bromide was a dibromide, m. p. 152°, which has since been shown by ultra-violet (Part I *) and infra-red (Corey, *J. Amer. Chem. Soc.*, **1954**, **76**, 175) spectroscopy to be the 5α : 7α-dibromo-derivative (I). Longer reaction produces an isomeric dibromide, m. p. 129°, which has been shown by the same means to be either the 5α : 7β- (II) or 5β : 7α-dibromide (III). Although the yield of each dibromide is only



about 40% it seems reasonable to assume with Corey (*loc. cit.*) that the *trans*-dibromide of m. p. 129° is formed by isomerisation of that of m. p. 152°. In his analysis of the stereochemistry of steroid α-bromo-ketones Corey (*loc. cit.*) assigned the configuration 5α : 7β to the stable dibromide, m. p. 129°, on the assumption that the isomerisation of the 5α : 7α-dibromide in the presence of hydrogen bromide must take place through acid-catalysed enolisation and cannot therefore involve the tertiary 5α-bromine atom. An equally likely mechanism for the isomerisation would be by reduction of the bromo-ketone by hydrogen bromide, followed by rebromination, and indeed Heilbron *et al.* (*loc. cit.*) showed that this very 5α : 7α-dibromo-ketone was reduced by hydrogen bromide in cold acetic acid to the 7α-monobromo-ketone. The isomerisation is in fact specifically catalysed by hydrogen bromide : the unstable dibromide is unchanged by even 7·5% perchloric acid in acetic acid after three days. This is consistant with the suggestion that the isomerisation takes place by the second mechanism, which also explains why the 5α : 7α-dibromide is stable to hydrogen bromide provided a large excess of bromine is present (Heilbron *et al.*, *loc. cit.*). Corey's reasoning is therefore fallacious.

Heilbron *et al.* acetolysed the *trans*-dibromide with potassium acetate in acetic acid to

* Part I, *J.*, 1954, 282.

a 3β : 5α-diacetoxy-7-bromocholestan-6-one which was reduced to 3β : 5α-diacetoxycholestan-6-one (IV). The ultra-violet absorption (see Table, No. 7) of this substance, $\Delta\lambda$ −6 mμ ($\Delta\lambda$ as defined in Part I), shows that it is 3β : 5α-diacetoxy-7β-bromocholestan-6-one (V) with an equatorial bromine atom. Fieser and Rajagopalan (*J. Amer. Chem. Soc.*, 1949, **71**, 3938) have already assigned this constitution to a compound obtained by bromination of 3β : 5α-diacetoxycholestan-6-one in the presence of boron trifluoride in acetic acid. The two isomers both give 3β : 5α-diacetoxycholestan-6-one on reduction with zinc dust in cold acetic acid and therefore differ only in the configuration at $C_{(7)}$. As required by the revised structure (VI), Fieser and Rajagopalan's bromo-ketone (No. 9) has $\Delta\lambda$ +27 mμ and the corresponding 5α-ol (No. 8) $\Delta\lambda$ +34 mμ, characteristic of an axial bromine atom. The unusually low extinction (cf. Part I) of the 5-acetate was not changed by further recrystallisation of the sample.

Although the 7α-bromide (VI) is stable to perchloric acid in acetic acid, it is isomerised by hydrogen bromide in acetic acid to the 7β-bromide (V). So, in this case at least, the isomerisation does involve reduction and rebromination, rather than simple acid-catalysed enolisation.

The fact that (VI), which would be an intermediate in the conversion of (III) into (V), is unchanged under the conditions of the acetolysis shows that the stable dibromide must have the alternative *trans*-configuration, 3β-acetoxy-5α : 7β-dibromocholestan-6-one (II). The isomerisations of (I) to (II) and of (VI) to (V) then become analogous. Although Heilbron *et al.* (*loc. cit.*) considered that the dibromide (I) could not be an intermediate in the formation of its isomer (II) since they could isolate only 3β-acetoxy-7α-bromocholestan-6-one after treatment of (I) with hydrogen bromide in acetic acid, there can now be little doubt that Corey (*loc. cit.*) is justified in regarding (I) as the kinetically controlled product of dibromination of 3β-acetoxycholestan-6-one and (II) as the thermodynamically controlled product. Retention of configuration in the acetolysis of (II) can plausibly be attributed to the intermediate formation of 3β : 6α-diacetoxy-7β-bromo-5β : 6β-epoxycholestane.

We take the opportunity of reporting the absorption spectra of some halogeno-derivatives of cholestan-2- and -3-one of known configuration recently prepared by Alt and Barton (*J.*, 1954, 4284) who kindly gave us samples (Nos. 10—14). The spectrum of 3α-bromocholestan-2-one (No. 12) is normal for an axial bromo-ketone. 3α-Chlorocholestan-2-one (No. 11) and 2β-chlorocholestan-3-one (No. 14) provided values of $\Delta\lambda$ for axial chlorine, which were lacking previously : as expected, chlorine causes a smaller shift than bromine.

The new measurements recorded in the Table combined with the absorption spectra of some 11 : 12-ketols recently published by Schindler and Reichstein (*Helv. Chim. Acta*, 1954, **37**, 667) show that the absorption of light by α-hydroxy- and α-acetoxy-ketones depends on the geometry of the systems, the effects being generally similar to those shown by α-bromo-ketones (Part I). Substitution of a hydroxyl group for an equatorial hydrogen atom shifts the maximum 12 mμ to shorter wave-length; an axial hydroxyl group causes a shift of 15—23 mμ to longer wave-length. An acetoxy-group shows $\Delta\lambda_e$ −5 mμ and $\Delta\lambda_a$ +7 to +11 mμ (subscripts refer to conformation). Since the parent, unoxygenated, ketone may not always be available for comparison perhaps a more useful generalisation is that acetylation of an equatorial 1-hydroxy*cyclo*hexanone moves the absorption maximum to a longer wave-length, while acetylation of an axial one moves the maximum to a shorter wave-length. By this criterion cevagenin (Nos. 28 and 29) is an equatorial α-ketol as proposed by Barton, Jeger, Prelog, and Woodward (*Experientia*, 1954, **10**, 81). Caudoside (No. 32), although undoubtedly an 11 : 12-ketol (Schindler and Reichstein, *loc. cit.*), appears to be an exception to the rule.

The reported maximum of methyl 3α-acetoxy-11-oxocholanoate (No. 16) seemed to be at an improbably long wave-length: a remeasurement of the light absorption of this substance showed that its maximum was in fact at the same position as that of the corresponding ætianate (No. 15). This revised value has been used in calculating the values of $\Delta\lambda$ for derivatives of 11-oxocholanic acid, which now fall into line with the other ketols in the Table. In a few examples calculation of $\Delta\lambda$ involves the assumption that

esterification of a carboxyl or hydroxyl in a remote part of the molecule does not change $\lambda_{max.}$. The axial 13-lactone group in the oleanolic acid series (Nos. 34 and 35) has an effect similar to that of an axial acetoxy-group.

$\Delta\lambda$ produced by introduction of hydroxyl, like that of chlorine and bromine (Part I),

No.	Compound	$\lambda_{max.}$ (in EtOH)	log ε	$\Delta\lambda_e$	$\Delta\lambda_a$	Ref.
1	3β-Acetoxycholestan-6-one	280	1·6	—	—	1, 2
		279	1·65	—	—	3
2	3β-Acetoxy-7α-bromocholestan-6-one	310	2·2	—	+30(Br)	1, 2
3	3β-Acetoxy-5α : 7α-dibromocholestan-6-one	340	2·2	—	+30(Br)	1, 2
		339	2·12	—	+30(Br)	3
4	3β-Acetoxy-5α : 7β-dibromocholestan-6-one, m. p. 129°	305	2·1	—	—	1, 2
		304	2·03	—	—	3
5	3β-Acetoxy-5α-hydroxycholestan-6-one	299·5	1·77	—	+20·5(OH)	3
6	3β : 5α-Diacetoxycholestan-6-one	290	1·93	—	+11(OAc)	3
7	3β : 5α-Diacetoxy-7β-bromocholestan-6-one	284	1·96	−6(Br)	—	3
8	3β-Acetoxy-7α-bromo-5α-hydroxycholestan-6-one	333·5	2·04	—	+34(Br) +23·5(OH)	3
9	3β : 5α-Diacetoxy-7α-bromocholestan-6-one	317	1·69	—	+27(Br) +7(OAc)	3
10	Cholestan-2-one	279·5	1·39	—	—	3
11	3α-Chlorocholestan-2-one	305	1·79	—	+25·5(Cl)	3
12	3α-Bromocholestan-2-one	312	2·04	—	+32·5(Br)	3
13	Cholestan-3-one	285	1·40	—	—	3
14	2β-Chlorocholestan-3-one	299·5	1·53	—	+14·5(Cl)	3
15	Methyl 3α-acetoxy-11-oxoætianate	297·5	1·44	—	—	4
16	Methyl 3α-acetoxy-11-oxocholanoate	305	1·50	—	—	5
		298	1·47	—	—	3
17	3α : 12α-Dihydroxy-11-oxocholanic acid	313	1·69	—	+15(OH)	6
18	Methyl 3α : 12α-diacetoxy-11-oxocholanoate	308	1·84	—	+10(OAc)	6
19	Methyl 3α : 12β-dihydroxy-11-oxocholanoate	285·5	1·67	−12·5(OH)	—	4
20	Methyl 3α : 12β-diacetoxy-11-oxocholanoate	294	1·47	−4(OAc)	—	4
		292	1·50	−6(OAc)	—	5
21	12-Oxocholanic acid	290	1·76	—	—	4
22	Methyl 3α-hydroxy-12-oxocholanoate	290	1·69	—	—	5
23	3α : 11α-Dihydroxy-12-oxocholanic acid	278	1·90	−12(OH)	—	4
24	Methyl 3α-acetoxy-11α-hydroxy-12-oxocholanoate	279	1·89	−11(OH)	—	4
25	Methyl 3α : 11α-diacetoxy-12-oxocholanoate	285	1·85	−5(OAc)	—	4
		285	1·87	−5(OAc)	—	5
26	Methyl 3α-acetoxy-11β-hydroxy-12-oxocholanoate	307	1·85		+17(OH)	4
		307	1·82	—	+17(OH)	5
27	Methyl 3α : 11β-diacetoxy-12-oxocholanoate	298·5	2·06	—	+8·5(OAc)	4
28	Cevagenin	279	1·71	—	—	3
29	Cevagenin *ortho*acetate diacetate	283	1·49	—	—	3
30	Sarmutoside	287	1·89	—	—	4
31	Sarmutogenin diacetate	293·5	1·94	—	—	4
32	Caudoside	295	1·76	—	—	4
33	Caudogenin diacetate	295	1·94	—	—	4
34	Methyl 3β-acetoxyolean-28-oate	287	1·47	—	—	3
35	12-Oxo-oleanolic lactone acetate	297	1·80	—	+10(lactone)	2
36	Camphor	289	1·51	—	—	3
37	3α-Hydroxycamphor	297·5	1·47	+8·5(OH)	—	3

1, Barr, Heilbron, Jones, and Spring, *J.*, 1938, **334**. 2, Cookson, *J.*, 1954, 282. 3, This paper. 4, Schindler and Reichstein, *Helv. Chim. Acta*, 1954, **37**, 667. 5, Wintersteiner, quoted in ref. 4. 6, Baumgartner and Tamm, quoted in ref. 4.

into a *cyclo*pentanone (Nos. 36—37) is intermediate between $\Delta\lambda_e$ and $\Delta\lambda_a$. The substance known as " α "-hydroxycamphor is assigned the *endo*-configuration, 3α-hydroxycamphor, since it is evidently the more stable epimer (Bredt and Fischer, *J. pr. Chem.*, 1931, **131**, 56; Lapworth and Chapman, *J.*, 1901, **79**, 384; cf. Part I).

Experimental

Ultra-violet absorption measurements were made in EtOH as described previously (Part I). Optical rotations were measured in $CHCl_3$ in a 1-dm. tube.

3β-Acetoxy-5α : 7α-dibromocholestan-6-one, made according to Heilbron, Jackson, Jones, and Spring (*J.*, 1938, 102), had m. p. 152—153°, $[\alpha]_D$ −140°. The isomeric dibromide, made by Woodward and Clifford's method (*J. Amer. Chem. Soc.*, 1941, **63**, 2727), had m. p. 129°, $[\alpha]_D$ −57°.

3β : 5α-*Diacetoxy*-7β-*bromocholestan*-6-*one*.—3β-Acetoxy-5α : 7β-dibromocholestan-6-one (m. p. 129°) (1·11 g.) was heated on the steam-bath for 7 hr. with freshly fused potassium acetate (2·2 g.) in acetic acid (100 ml.). The mixture was then diluted with water, and the precipitate recrystallised thrice from acetic acid, to give the diacetate, m. p. 198—199° (248 mg.). When reaction was for only 1·5 hr., as described by Heilbron *et al.* (*loc. cit.*), only unchanged dibromide could be isolated by crystallisation.

3β : 5α-*Diacetoxy*-7α-*bromocholestan*-6-*one*.—Prepared according to Fieser and Rajagopalan (*J. Amer. Chem. Soc.*, 1949, **71**, 3938), 3β-acetoxy-5α-hydroxy-7α-bromocholestan-6-one had m. p. 170—171°, $[\alpha]_D$ +7°, and its 5-acetate, m. p. 215—216°, $[\alpha]_D$ +39°.

Reduction with Zinc and Acetic Acid.—3β : 5α-Diacetoxy-7β-bromocholestan-6-one (42 mg.) was dissolved in warm acetic acid (5 ml.). When the solution had cooled to room temperature zinc dust was added in portions to the stirred mixture during 3 hr. Next day the filtered solution was diluted with water, and the precipitate crystallised twice from methanol. The m. p. of the resulting needles, 170—171°, was unchanged when they were mixed with an authentic sample of 3β : 5α-diacetoxycholestan-6-one of the same m. p.

The 7α-epimer gave the same product on reduction.

Epimerisation of 3β : 5α-*Diacetoxy*-7α-*bromocholestan*-6-*one*.—A solution of 3β : 5α-diacetoxy-7α-bromocholestan-6-one (55 mg.) in acetic acid (15 ml.) containing hydrogen bromide (5%) was left at room temperature for 40 hr. The mixture was then poured into water, and the precipitate collected, washed with water, and recrystallised twice from acetic acid. The resulting crystals (25 mg.) melted at 201—202°, alone or mixed with 3β : 5α-diacetoxy-7β-bromocholestan-6-one made by acetolysis of the 5α : 7β-dibromide.

When perchloric acid was substituted for hydrogen bromide the 7α-isomer was recovered under the above conditions. It was also unchanged by 9 hours' heating on the steam-bath with potassium acetate in acetic acid.

We are grateful to Professor D. H. R. Barton, F.R.S., for his helpful interest and for generously putting his collection of steroid and triterpenoid samples at our disposal.

Birkbeck College, London, W.C.1. [*Received, September 29th*, 1954.]

Polysaccharides of Baker's Yeast. Part I. Glycogen.

By Stanley Peat, W. J. Whelan, and T. E. Edwards.

[Reprint Order No. 5780.]

The method of "linkage analysis" of polysaccharides which involves the partial acid hydrolysis of a polysaccharide and the isolation (and characterisation) of the oligosaccharide fragments by charcoal chromatography has been applied to yeast glycogen and has resulted in the detection of only α-1 : 4- and α-1 : 6-types of glucosidic linkage. An essential part of the proof has consisted in the separation and isolation of maltose and *iso*maltose from the acid hydrolysate, readily accomplished on a charcoal column. The conclusion is reached that most, if not all, of the branch linkages are 1 : 6-links in the α-configuration.

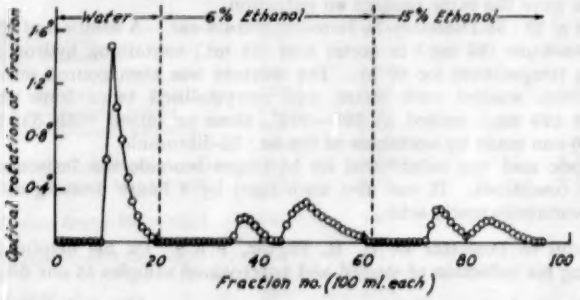
Our researches over a number of years have been concerned with the metabolism of starch and related polysaccharides in the higher plants. Cognate studies of the maltase and invertase of yeast have renewed our interest in the polysaccharides of yeast and in particular in the problem of the inter-relation which might exist between the cell-wall polysaccharides, mannan and glucan, and the glycogen. This first communication reports the results of a structural analysis of the glycogen of baker's yeast. The earlier literature contains suggestions of the existence of two glycogens in yeast but Northcote (*Biochem. J.*, 1953, **53**, 348) has presented evidence which disposes of this misconception.

One of the most satisfactory methods of what might be called "linkage-analysis" of

branched polysaccharides consists in the partial hydrolysis of the polysaccharide by acid and the isolation and characterisation of the oligosaccharide fragments so produced. As has been pointed out by Whistler and Smart ("Polysaccharide Chemistry," Academic Press, New York, 1953) the method is free from the dubiety which attaches to assays based upon methylation or upon periodic acid oxidation. The classical method of hydrolysis of the methylated polysaccharide and characterisation of the resulting partly methylated monosaccharides has always been open to the very serious objection that it is rarely possible to achieve complete methylation of all the free hydroxyl groups in a large polysaccharide molecule. The objection to the less laborious periodate method lies in the difficulty experienced in controlling the reaction and estimating the extent of over- or under-oxidation in a given set of circumstances.

In the method of partial acid hydrolysis, the possibility of reversion synthesis of di- and tri-saccharides exists but does not detract from the value of the method since conditions of hydrolysis can usually be found under which reversion synthesis is insignificant in extent. The method obviously depends on quantitative separation of the oligosaccharides produced by fragmentation of the polysaccharides. The technique used for this purpose is

FIG. 1. *Fractionation of glycogen hydrolysate on charcoal–Celite.*



chromatographic separation on charcoal, originated by Whistler and Durso (*J. Amer. Chem. Soc.*, 1950, **72**, 677).

So far as we are aware, the only structural analysis hitherto made of yeast glycogen is that reported by Northcote (*loc. cit.*). The procedure adopted by this author included (i) end-group assay by the methylation (Haworth) and the periodate method, (ii) examination of the acid hydrolysate of the methylated glycogen, and (iii) study of the β-amylolysis of the polysaccharide. In none of these particulars was the yeast glycogen distinguishable from animal glycogens. It possesses a highly branched structure; the chain-forming linkages are 1 : 4-glucosidic and the average basal chain length * is 12 glucose units. Branching was indicated by the existence of a β-amylolysis limit at 50% conversion and by the isolation of a di-*O*-methylglucose fraction from the hydrolysate of the methylated glycogen. Paper chromatograms suggested the presence of two di-*O*-methylglucoses but neither was identified. The type or types to which the branch linkages belong remained therefore undetermined.

In our experiments the glycogen was extracted by acetic acid from fresh baker's yeast, by Northcote's procedure (*loc. cit.*), and was submitted to partial hydrolysis (with sulphuric acid) equivalent to 75% conversion into glucose. The neutralised hydrolysate was then separated on a charcoal column (cf. Whelan, Bailey, and Roberts, *J.*, 1953, 1293). Examination of the fractions (see Fig. 1) demonstrated the occurrence of one monosaccharide, two disaccharides, and at least three trisaccharides. The sugars were isolated and converted into the corresponding acetates, the properties of which are recorded in the

* The use of the term "chain length" in connection with a randomly branched polymer is misleading. The so-called chain length of a branched polysaccharide is measured by the percentage of non-reducing end groups and actually represents the number of monosaccharide units per end group. We describe this quantity as "basal chain length."

Table. The monosaccharide fraction, obtained by irrigation of the column with water, consisted of D-glucose only. The disaccharide fraction, eluted by 6% aqueous ethanol, contained two members which were identified by comparison with authentic specimens (see Table) as maltose and *iso*maltose (Fig. 2*b* and *c*). It should be observed (Fig. 1) that a sharp separation of these two sugars, not otherwise easily separable, is achieved on

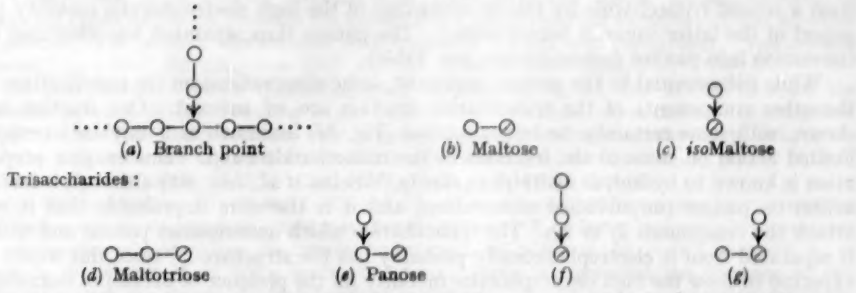
Properties of the products of hydrolysis of baker's yeast glycogen.

Sugar	Yield * (g.)	Characterising derivative	Properties of derivatives † $[\alpha]_D$	m. p.
[Glycogen]	[4·49]			
Glucose	2·45	Sugar	+52·7° (52·6°)	144° (146°)
*iso*Maltose	0·165	Octa-acetate	+96·8 (97)	143—144 (143—144)
Maltose	0·980	Octa-acetate	+62·7 (+63)	158—159 (159—160)
Panose	—	Panitol dodeca-acetate	+119 (+120)	146—147 (148—150)

* Calc. by summation of optical rotations of fractions obtained from the charcoal column (see Experimental section).

† Values found for authentic specimens are given in parentheses.

FIG. 2. *Oligosaccharides from Yeast Glycogen.*



○ = glucopyranose unit; ⊘ = reducing glucose unit; — = α-1 : 4-link; ↓ = α-1 : 6-link.

charcoal. These being the only disaccharide products it may be concluded that only two types of glycosidic linkage exist in yeast glycogen, namely, α-1 : 4- and α-1 : 6-linkages. The importance has already been stressed of providing proof that the oligosaccharides obtained in this type of experiment do not arise from the acid-catalysed polymerisation of the monosaccharide and we have satisfied ourselves by control experiments, which will be described in a later paper, that neither the maltose nor the *iso*maltose obtained from yeast glycogen is an artifact of this kind.

The yields (see Table) of maltose and *iso*maltose were in the approximate ratio of 6 : 1. The ratio of α-1 : 4- to α-1 : 6-linkages in yeast glycogen can be estimated from Northcote's end-group assay (*loc. cit.*) as approximately 11 : 1. The fact that *iso*maltose thus accumulates preferentially with respect to maltose is due to the greater stability of the α-1 : 6-linkage. Wolfrom, Lassettre, and O'Neill (*J. Amer. Chem. Soc.*, 1951, **73**, 595) have shown that at 100° the rates of hydrolysis of maltose and *iso*maltose by acid are in the ratio 4 : 1. These authors have also made calculations of the amounts of *iso*maltose to be expected at various stages in the hydrolysis of rabbit-liver glycogen which has the same proportion of branch linkages as the yeast glycogen. Their calculations show that at 75% hydrolysis (the limit to which our glycogen was taken) the yield of *iso*maltose should be 259 mg. from 4·49 g. We obtained only 165 mg. and this lower yield is known not to be caused by losses during fractionation. This suggests that the relative strength of the linkages in *iso*maltose and maltose is not the same as that of the α-1 : 6- and α-1 : 4-links in the polysaccharide.

The identification of maltose as one of the major products of partial hydrolysis agrees with Northcote's conclusions (*loc. cit.*) and proves that the 1 : 4-glucosidic links have the α-configuration. The isolation of *iso*maltose is consistent with the idea of a branched molecule in which the branch links are of the α-1 : 6-type. It should be noted, however,

that the isolation of maltose and *iso*maltose does not prove that the glycogen of yeast possesses a branched structure.

Conclusive evidence that α-1 : 4- and α-1 : 6-linkages actually occur together in the same molecule was afforded by the isolation and identification of panose (Fig. 2*e*) as a constituent of the trisaccharide fraction eluted from the charcoal column by 15% ethanol. Although panose could be derived from an unbranched polyglucose in which the glucosidic linkages were of two types (α-1 : 4 and α-1 : 6), nevertheless the clear demonstration by Northcote (*loc. cit.*) of the branched character of the yeast glycogen molecule makes it more reasonable to regard the panose which we have isolated as arising from the branched structure represented in Fig. 2*a*.

The number of trisaccharides theoretically derivable by random hydrolysis of a polysaccharide constituted as in Fig. 2*a* is four. One of these, maltotriose (Fig. 2*d*) contains α-1 : 4-links only. The remaining three trisaccharides contain both the α-1 : 4- and the α-1 : 6-link (Fig. 2*e*, *f*, and *g*). Indications were given in our experiments of the presence in the trisaccharide fraction of three of the four possible components and one of these was proved to be panose (Fig. 2*e*). Complete separation of the trisaccharides was not attempted on the charcoal column, and the panose component was ultimately separated from a second trisaccharide by taking advantage of the high electrophoretic mobility (on paper) of the latter sugar in borate buffer. The panose thus separated was identified by conversion into panitol dodeca-acetate (see Table).

While not essential to the present argument, some observations on the constitutions of the other components of the trisaccharide fraction are of interest. One fraction was shown, with some certainty, to be maltotriose (Fig. 2*d*) inasmuch as β-amylase exerted a limited action on some of the fractions in the trisaccharide band. This enzyme preparation is known to hydrolyse maltotriose slowly (Whelan *et al.*, *locc. cit.*) although it has no action on panose (unpublished observation) and it is therefore improbable that it will attack the compounds 2*f* or 2*g*. The trisaccharide which accompanies panose and which is separated from it electrophoretically probably has the structure 2*f*, since this would be expected to show the high electrophoretic mobility (in the presence of borate) of *iso*maltose rather than the low mobility of maltose (cf. Foster, *J.*, 1953, 982).

It is concluded from these experiments taken in conjunction with those of Northcote (*loc. cit.*) that the glycogen from baker's yeast possesses the branched structure which is now commonly accepted for glycogen whatever its source. A rigid experimental proof that the branch linkage is of the α-1 : 6-type has however been afforded by this method in only one other case, namely, for rabbit-liver glycogen. From the latter, by partial acid hydrolysis, maltose and *iso*maltose were obtained (Wolfrom *et al.*, *loc. cit.*). Panose was not isolated in this experiment; indeed, our preparation of panose is the first recorded isolation of this trisaccharide from a glycogen.

By an alternative procedure, namely, application of the method of Hirst, Jones, and Roudier (*J.*, 1948, 1779) to glycogen from a number of other biological sources, Bell and Manners (*J.*, 1954, 1891) have shown that more than 99% of the branch linkages in these glycogens are 1 : 6-links.

Experimental

Preparation of Glycogen.—The glycogen was prepared from fresh baker's yeast (Distillers Co. Ltd.). The alkali-insoluble residue was prepared from the yeast as by Bell and Northcote (*J.*, 1950, 1944) and glycogen was extracted from this with hot dilute acetic acid as follows. The alkali-insoluble residue (112 g.; from 6 kg. of pressed yeast) was treated with 0·5N-acetic acid (2 l.) at 75° for 1 hr., cooled, and centrifuged, and the gelatinous solid stirred with water (2 × 1·5 l.) at 75—80° for 1 hr. The combined extracts were treated with ethanol (2 vol.) at 4° and the precipitated glycogen was removed, washed with ethanol, and dried *in vacuo* over phosphoric oxide at room temperature (yield, 3·44 g.). The insoluble residue (67 g.), which was being used as a source of yeast glucan, was extracted a further four times with hot water as above but still appeared to contain some glycogen. It was therefore re-extracted with acetic acid as above and there was obtained a further 3·64 g. of glycogen which was combined with the first batch. Acidic hydrolysis of the polysaccharide after drying at 60° *in vacuo* over phosphoric oxide yielded 99·0% of glucose (Pirt and Whelan's method,

J. Sci. Food Agric., 1951, **2**, 224). The $[\alpha]_D$ in water was +188·7° (*c*, 0·1086, based on glucose content); ash content, nil (Found: N, nil).

Hydrolysis of the Glycogen.—Glycogen (approx. 5 g.; undried) was weighed into a 250-ml. flask, wetted with ethanol, and dissolved by gentle warming in 0·1N-sodium hydroxide (100 ml.). The solution was neutralised with sulphuric acid, 5N-acid (16·7 ml.) added, and the solution diluted to 250 ml., the final concentration of acid being 0·33N. A portion (1 ml.) was removed for determination of the glycogen content (Pirt and Whelan, *loc. cit.*) which was found to be 4·58 g. The remainder of the solution was heated in a boiling-water bath, portions (1 ml. each) were removed at intervals, neutralised, and diluted to 25 ml., and the reducing powers (as glucose) of 3 ml. portions were determined with the Somogyi copper reagent (*J. Biol. Chem.*, 1945, **160**, 61). After being heated for 170 min. the solution was cooled and at this stage the reducing power corresponded to an apparent conversion into glucose of 75%.

Fractionation of Products of Hydrolysis.—The acid hydrolysate (245 ml., equiv. to 4·49 g. of glycogen) was neutralised (6N-sodium hydroxide) and added to a charcoal–Celite column (adsorbent, 3·5 × 80 cm.) which was prepared and eluted as described by Whelan *et al.* (*loc. cit.*). The optical rotation of each fraction (100 ml.) was measured in a 4-dm. tube and the results are shown in Fig. 1. Fractions nos. 10—20, 34—41, 44—60, 71—75, 76—80, 81—82, 83—85, and 86—92 were combined and evaporated to dryness under reduced pressure.

Examination of Hydrolysis Products.—(a) *Monosaccharide.* Paper chromatography of combined fractions 10—20 revealed the presence of a single reducing sugar having the R_F value of glucose. The product was refluxed with methanol, filtered, and crystallised. The crystals showed $[\alpha]_D$ +87·1° (35 min.) ⟶ 52·7° (4·75 hr.) in water (see Table).

(b) *Disaccharides.* Paper chromatography of fractions 34—41 and 44—60 revealed the presence in each of one reducing sugar having the R_F values of *iso*maltose and maltose respectively. The β-octa-acetates were prepared by using sodium acetate–acetic anhydride, and the properties are reported in the Table (Found: *iso*maltose acetate, C, 49·4; H, 5·6; maltose acetate, C, 49·6; H, 5·7. Calc. for $C_{28}H_{38}O_{19}$: C, 49·5; H, 5·6%).

(c) *Trisaccharides.* Fractions 71—75 and 76—80 were examined by paper chromatography and their contents migrated as single spots having the same R_F value as panose. Fractionation by electrophoresis on paper in borate buffer (pH 8·7; 9·9 g. of H_3BO_3 + 22·88 g. of $Na_2B_4O_7,10H_2O$ per l.) at 400 v (current, 7·5 mA; temp. 4°) revealed the presence of two reducing sugars, the slower of which behaved as panose. The fractions were combined and the two sugars separated by electrophoresis on Whatman no. 3 filter paper, the sugar mixture (approx. 200 mg.) being applied as a narrow streak along a 40-cm. line at right angles to the electric field on each of two papers (46 × 57 cm.). The apparatus used in electrophoresis was constructed from "Perspex" according to Latner (*Biochem. J.*, 1952, **51**, xii). After electrophoresis for 48 hr. at 4° (400 v; 6·5—9 mA) the positions of the sugars were located by spraying guide strips with benzidine–trichloroacetic acid (Bacon and Edelman, *Biochem. J.*, 1951, **48**, 114). The sugars were isolated by extracting the appropriate sections of the papers with water (3 × 200 ml.) and evaporating the extracts to dryness under reduced pressure. The faster-moving component was not further examined. The slower-moving component was dissolved in water (2 ml.), mixed with potassium borohydride solution (1 ml.; 30 mg.), and left for 2 hr. at room temperature. The solution was acidified with acetic acid to destroy excess of borohydride, neutralised, evaporated to dryness, and acetylated as above, yielding an acetate (94 mg.) having properties identical with those of panitol doceca-acetate (see Table) (Found: C, 50·2; H, 6·1. Calc. for $C_{42}H_{58}O_{28}$: C, 49·9; H, 5·8%).

Fractions 81—82, 83—85, and 86—92 were examined by paper chromatography; 81—82 contained two zones migrating with panose and maltotriose, fractions 83—85 and 86—92 each contained two zones migrating with maltotriose and maltotetraose. Each group of fractions was treated with a concentrated solution of crystalline sweet potato β-amylase (kindly provided by Dr. A. K. Balls) and left for 7 days at 35° under toluene. Paper-chromatographic examination of the digests revealed that substances having the R_F values of glucose and maltose had been produced from fractions 81—82 and 83—85; none of the original zones had completely disappeared.

The authors thank Professor M. L. Wolfrom for a gift of *iso*maltose β-octa-acetate, Dr. S. C. Pan for a sample of panose, Imperial Chemical Industries Limited for the loan of a polarimeter, and the Department of Scientific and Industrial Research for a maintenance grant (to T. E. E.).

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Chromium Phosphates: Phase-diagram and Preliminary Ion-exchange Studies of the System: Chromic Oxide–Phosphoric Oxide–Water at 0° and 40°.

By R. F. Jameson and J. E. Salmon.

[Reprint Order No. 5781.]

Two series of compounds, one purple (derived from the hexaquochromic ion) and the other green (containing complex phosphatochromic ions), have been found to occur in the system chromic oxide–phosphoric oxide–water. A phase-diagram study of the system at 0°, where both solutions and solids were purple, has shown that in the range of solutions containing from 1% to 52% of phosphoric oxide the following are the stable solid phases: $Cr_2O_3,P_2O_5,12H_2O$; $2Cr_2O_3,3P_2O_5,51H_2O$; $Cr_2O_3,2P_2O_5,19H_2O$; $Cr_2O_3,3P_2O_5,18H_2O$. At 40°, when the solutions and solids were green, the following were found to be the stable solid phases in contact with solutions containing between 1% and 56% of phosphoric oxide: $Cr_2O_3,P_2O_5,12H_2O$; $Cr_2O_3,2P_2O_5,8H_2O$; $Cr_2O_3,3P_2O_5,10H_2O$. Attempts to study the system at 25° were abandoned since both solutions and solids remained indefinitely in a state between the green and the purple forms.

Ion-exchange experiments at 0° have shown the hexaquochromic ion to be the only species adsorbed by the cation-exchanger, and phosphate ions the only ones adsorbed by the anion-exchanger. The molar amounts of phosphate adsorbed per equivalent of resin from the chromic phosphate solutions were the same as from phosphoric acid solutions of similar concentrations. At 40° the adsorption of both anionic and cationic complexes was observed. Preliminary studies indicated these to be $[Cr(PO_4)_2,aq.]^{3-}$ and $[Cr(HPO_4),aq.]^{+}$ respectively.

No systematic study appears to have been made previously of the chromic phosphates, although several solid chromic phosphates have been reported. Thus both a green and a purple modification of the tertiary phosphate are known. The latter has been described by, *e.g.*, Rammelsberg (*Pogg. Annalen*, **1846**, **68**, 149), Glühmann (*Annalen*, **1848**, **65**, 149), Joseph and Rae (*J.*, **1917**, **111**, 196), and Ness, Smith, and Evans (*J. Amer. Chem. Soc.*, 1950, **72**, 2813). All these workers formulated it as $Cr_2O_3,P_2O_5,12H_2O$ (or $CrPO_4,6H_2O$) and observed that it occurred as purple, hexagonal crystals (a description that accords with the present observations). A lavender-coloured amorphous variety has also been described by Rammelsberg and by Joseph and Rae (*locc. cit.*).

The degree of hydration of the green form was stated by Rammelsberg (*loc. cit.*) to be the same as for the purple modification, but Joseph and Rae (*loc. cit.*) ascribed it eight molecules of water, *viz.*, $Cr_2O_3,P_2O_5,8H_2O$.

The only other salt of orthophosphoric acid described is the compound $Cr_2O_3,2P_2O_5,19H_2O$, for which Haushofer (*Z. Krist.*, **1883**, **7**, 263) has given goniometric measurements; the colour of this compound was said to be the same as that of chrome alum.

The original aim of the present work was to determine the solubility isotherm of the system chromic oxide–phosphoric oxide–water at 25°, but a difficulty was encountered in that at this temperature both solutions and solids remained indefinitely in a state intermediate between the purple and the green forms (the solids being mechanical mixtures) without, apparently, reaching equilibrium. However, it proved possible to obtain data for the appropriate phase diagrams at both 0° and 40° where both solutions and solids remained purple and emerald-green respectively.

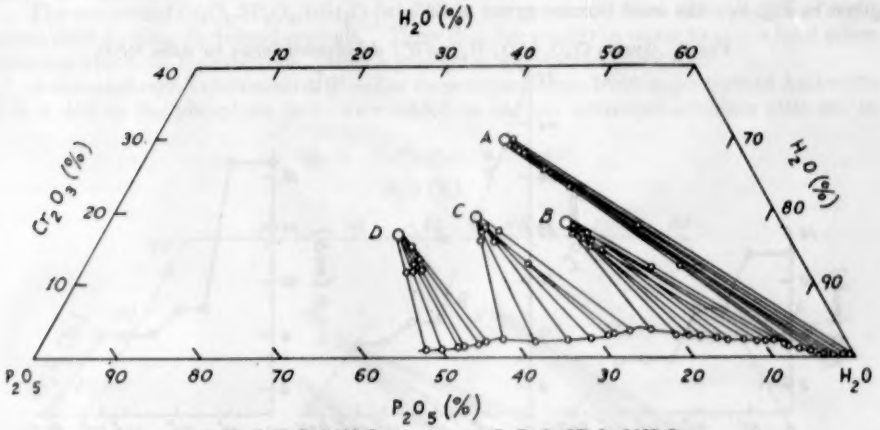
Results.

Phase-diagram Studies at 0°.—A study of the system at 0° for the range of solutions up to 52% of phosphoric oxide has indicated the following as the stable solid phases (Table 1, Fig. 1): (*A*) $Cr_2O_3,P_2O_5,12H_2O$, as dull-purple, hexagonal plates, (*B*)

$2Cr_2O_3,3P_2O_5,51H_2O$, as black, irregular-shaped crystals, (*C*) $Cr_2O_3,2P_2O_5,19H_2O$, as purple, hexagonal-sectioned crystals, and (*D*) $Cr_2O_3,3P_2O_5,18H_2O$, as bright purple crystals.

Samples of the tertiary salt, $Cr_2O_3,P_2O_5,12H_2O$, were heated to constant weight at several temperatures and the loss in weight recorded. The results, which are plotted in Fig. 2*a*, differ from those of Joseph and Rae in showing a break in the curve corresponding

FIG. 1. Cr_2O_3–P_2O_5–H_2O *at* 0°.



A, $Cr_2O_3,P_2O_5,12H_2O$. *C*, $Cr_2O_3,2P_2O_5,19H_2O$.
B, $2Cr_2O_3,3P_2O_5,51H_2O$. *D*, $Cr_2O_3,3P_2O_5,18H_2O$.

TABLE 1. *The system chromic oxide–phosphoric oxide–water at* 0°.

Solutions			Moist solids			Solutions			Moist solids		
P_2O_5 (%)	Cr_2O_3 (%)	$[PO_4]/[Cr]$	P_2O_5 (%)	Cr_2O_3 (%)	Type *	P_2O_5 (%)	Cr_2O_3 (%)	$[PO_4]/[Cr]$	P_2O_5 (%)	Cr_2O_3 (%)	Type *
0·981	0·101	10·4	27·62	29·23		25·66	3·53	7·80	34·83	17·56	
1·352	0·153	9·45	26·19	28·00		28·01	3·18	9·43	36·47	17·88	
2·50	0·325	8·25	26·62	28·53		28·41	3·19	9·55	33·31	12·80	
3·76	0·578	6·97	17·65	17·67		30·98	2·91	11·4	35·89	16·22	*C*
4·47	0·647	7·40	22·81	23·83	*A*	33·90	2·65	13·7	36·00	15·48	
5·09	0·933	5·85	—	—		38·06	2·54	16·1	36·87	17·44	
6·22	1·31	5·11	24·88	26·02		41·96	2·53	17·8	37·56	16·22	
7·48	1·68	4·78	24·23	25·54							
7·59	1·77	4·61	14·96	12·59		44·03	1·95	24·2	46·72	15·32	
		†				44·91	1·86	25·9	46·51	13·46	
8·99	2·24	4·31	18·71	12·23		47·23	1·48	34·2	47·00	11·73	*D*
9·88	2·24	4·74	24·42	17·00		47·41	1·47	34·6	47·51	12·56	
10·81	2·36	4·91	23·11	14·84		49·79	1·26	42·3	48·18	11·74	
12·42	2·53	5·26	24·44	15·85		51·77	1·17	47·4	48·77	11·65	
14·22	2·77	5·50	25·40	18·01							
15·68	2·87	5·86	25·03	17·05	*B*						
17·85	3·03	6·31	25·57	17·72							
18·70	3·13	6·41	25·01	16·68							
20·21	3·26	6·64	24·66	15·61							
23·22	3·77	6·58	26·03	17·13							

* Where *A* = $Cr_2O_3,P_2O_5,12H_2O$;
B = $2Cr_2O_3,3P_2O_5,51H_2O$;
C = $Cr_2O_3,2P_2O_5,19H_2O$;
D = $Cr_2O_3,3P_2O_5,18H_2O$.

† The minimum value of the mol. ratio occurs at this transition point.

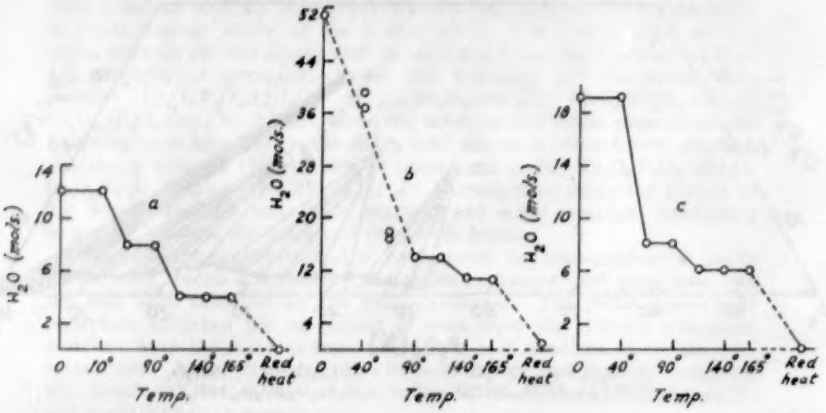
to the formation of $Cr_2O_3,P_2O_5,8H_2O$ (at which point the solid becomes green), but these authors carried out their experiments in a dry atmosphere, whereas the present work was carried out under normal atmospheric conditions of humidity.

The compound $2Cr_2O_3,3P_2O_5,51H_2O$ has not been described before, and its degree of hydration cannot be fixed accurately by examination of the tie-lines (Fig. 1); the formula was decided on the basis of an examination of the phase diagram in conjunction with the results of experiments in which the compound was dried at various temperatures (see

Fig. 2*b*). The compound started to lose water rapidly at 40°, at which point it became partly green, but at each temperature it took too long to reach constant weight until a temperature of 95° was used; the solid was then wholly green. The loss of water at each break in the curve (Fig. 2*b*) corresponded to integral numbers of water molecules (*viz.*, 11 and 14 remain) when the original compound was assumed to contain 51 molecules of water.

The compound $Cr_2O_3,2P_2O_5,19H_2O$ has been described before by Haushofer (*loc. cit.*) and his description of it accords with the present observations. A dehydration curve is given in Fig. 2*c*; the solid became green at 65°.

FIG. 2. *System* Cr_2O_3–P_2O_5–H_2O *at* 0°; *dehydration curves for stable solids.*



(*a*) $Cr_2O_3,P_2O_5,12H_2O$. (*b*) $2Cr_2O_3,3P_2O_5,51H_2O$. (*c*) $Cr_2O_3,2P_2O_5,19H_2O$.

The compound $Cr_2O_3,3P_2O_5,18H_2O$ has not been described before. It forms bright purple crystals that dissolve readily in water to give a pale solution that gradually deposits hexagonal crystals similar in appearance to those of the tertiary salt. It is very hygroscopic.

Phase-diagram Studies at 40°.—The chromic phosphate system at 40° has been studied for the range of solutions containing up to 56% of phosphoric oxide and the following stable solid phases identified (Table 2, Fig. 3): (*E*) $Cr_2O_3,P_2O_5,12H_2O$, as a pale green, microcrystalline solid, (*F*) $Cr_2O_3,2P_2O_5,8H_2O$, as a dark green, semicrystalline solid, and (*G*) $Cr_2O_3,3P_2O_5,10H_2O$, as a bright green, crystalline solid.

TABLE 2. *The system chromic oxide–phosphoric oxide–water at* 40°.

Solutions			Moist solids			Solutions			Moist solids		
P_2O_5 (%)	Cr_2O_3 (%)	$[PO_4]/[Cr]$	P_2O_5 (%)	Cr_2O_3 (%)	Type *	P_2O_5 (%)	Cr_2O_3 (%)	$[PO_4]/[Cr]$	P_2O_5 (%)	Cr_2O_3 (%)	Type *
0·870	0·051	18·1	21·22	22·48		20·72	8·95	2·48	41·36	21·32	
1·932	0·143	14·4	26·13	27·89		22·45	8·20	2·94	36·21	17·46	
3·44	0·340	10·9	26·44	28·51		25·24	7·43	3·61	33·05	13·55	
4·22	0·494	9·16	20·69	21·48		29·87	7·10	4·51	39·66	16·31	
7·43	1·24	6·44	20·38	19·50		33·01	7·43	4·76	—	—	*F*
9·22	1·57	6·29	22·51	21·23	*E*	35·35	7·82	4·84	42·61	17·72	
11·13	2·66	4·48	21·96	21·52		38·83	8·44	4·93	44·98	19·03	
12·63	3·77	3·59	20·49	16·73		41·96	9·39	4·79	46·21	20·68	
15·88	6·18	2·75	18·89	12·53		43·11	9·81	4·71	46·99	19·60	
17·34	8·34	2·23	20·13	14·03							
18·84	9·19	2·19	23·41	20·39		45·63	10·38	4·71	49·46	14·43	
		↑				47·21	8·61	5·88	50·81	13·48	
						49·11	7·57	6·95	53·93	15·86	
						50·54	6·71	8·07	52·38	11·85	*G*
						51·76	5·97	9·28	53·89	12·67	
						54·89	5·07	11·6	55·38	10·80	
						56·13	4·98	12·1	56·00	9·23	

* Where *E* = $Cr_2O_3,P_2O_5,12H_2O$;
F = $Cr_2O_3,2P_2O_5,8H_2O$;
G = $Cr_2O_3,3P_2O_5,10H_2O$.

† The minimum value of the mol. ratio occurs at this transition point.

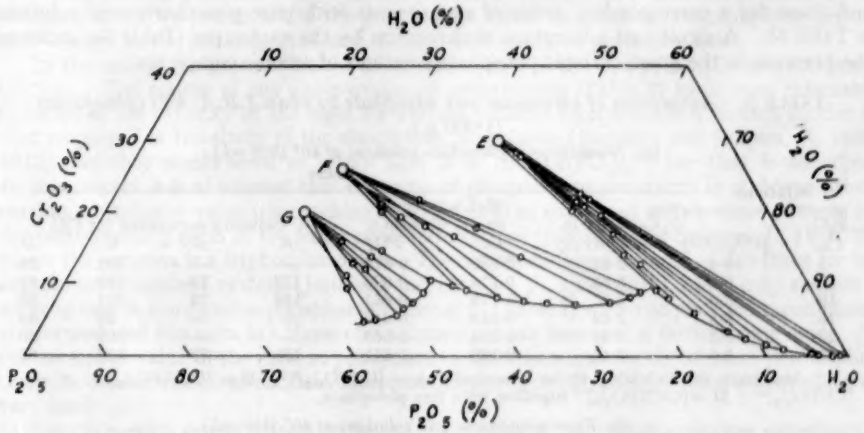
The tertiary salt, $Cr_2O_3,P_2O_5,12H_2O$, is stable towards water and exhibits no discernible crystal pattern.

The compound $Cr_2O_3,2P_2O_5,8H_2O$, has not previously been described. It is a dark green solid forming large ill-shaped crystals having only two well-defined faces and exhibiting conchoidal fracture. It is insoluble in water. A green compound of the same composition makes its appearance during the dehydration of the purple salt $Cr_2O_3,2P_2O_5,19H_2O$ (see Fig. 2*c*).

The compound $Cr_2O_3,3P_2O_5,10H_2O$ (which has not previously been described) is a bright green solid forming ill-defined crystals. These dissolve readily in water to give a light green solution which, on high dilution, yields a pale green amorphous precipitate.

Anion-exchange Experiments at 0°.—For these experiments 1·000-g. portions of Amberlite I.R.A.-400 in the phosphate form were added to various saturated solutions (100 ml. in

FIG. 3. Cr_2O_3–P_2O_5–H_2O *at* 40°.



E, $Cr_2O_3,P_2O_5,12H_2O$. *F*, $Cr_2O_3,2P_2O_5,8H_2O$. *G*, $Cr_2O_3,3P_2O_5,10H_2O$.

each case) and left, with daily shaking, for three weeks. The solutions were prepared from 5M-phosphoric acid, the tertiary salt, and water according to the previously determined solubility isotherm.

The results, which are given in Table 3, show that no chromium was adsorbed on to the exchanger, but phosphate only, and that the amount of phosphate adsorbed was the same as that from pure phosphoric acid solutions of the same concentration (cf. Table 5*b*).

TABLE 3. *Adsorption of phosphate by resin I.R.A.-400 (phosphate) (1·000 g.) from chromic phosphate solutions at* 0° *(100 ml.).*

Solutions		Resin	
P_2O_5 (%)	$[PO_4]/[Cr]$	Capacity (m. equiv./g.)	Mol. of PO_4 * adsorbed per equiv. of resin
5	5·87	2·32	0·660
10	4·68	2·44	0·620
15	5·91	2·44	0·625
20	6·60	2·49	0·622

* No chromium was adsorbed.

Cation-exchange Experiments at 0°.—The results of similar experiments with the hydrogen form of the cation-exchanger Zeo-Karb 225 are given in Table 4. No adsorption of phosphate was observed and the adsorption of the tervalent chromium ion was almost independent of the pH. The exchanger was never completely saturated with the chromium ions and this was probably due to the blocking of some of the exchange sites by the large hexaquochromic ion, in which form it is most likely that the chromium is adsorbed.

TABLE 4. *Adsorption of chromium by Zeo-Karb 225-H (0·500 g.) from chromic phosphate solutions at 0° (100 ml.).*

Solutions			Resin	
P_2O_5 (%)	$[PO_4]/[Cr]$	pH	Capacity (m. equiv./g.)	Mol. of Cr * adsorbed per equiv. of resin
5	5·87	1·56	3·57	0·329
10	4·68	1·40	3·59	0·323
15	5·91	1·01	3·59	0·318
20	6·60	0·68	3·59	0·309

* No phosphate was adsorbed.

Anion-exchange Experiments at 40°.—The adsorption of chromium and phosphate by Amberlite I.R.A.-400 (in the phosphate form) from stable solutions (*i.e.*, of compositions decided on the basis of the solubility isotherm at 40°; since the solutions were made up from the purple tertiary salt they were initially aged at 40° for approximately three weeks) has been determined under equilibrium conditions. The results are given in Table 5*a* and those for a corresponding series of experiments with pure phosphoric acid solutions in Table 5*b*. A significant adsorption of chromium by the exchanger (Table 5*a*) indicates the presence in the green chromic phosphate solutions of anionic complexes.

TABLE 5. *Adsorption of chromium and phosphate by resin I.R.A.-400 (phosphate) (1·000 g.).*

(*a*) *From chromic phosphate solutions at 40° (100 ml.).*

Solutions		Resin						
P_2O_5 (%)	$[PO_4]/[Cr]$	Capacity in (m. equiv./g)	Mol. adsorbed/ equiv. of resin : Cr	PO_4	Capacity accounted for (%) * A	B	C	D
1	16·4	2·44	0·232	0·677	—	—	102	56
5	8·6	2·44	0·174	0·676	127	75	102	67
10	5·0	2·37	0·173	0·661	125	73	101	66
15	2·8	2·48	0·219	0·649	—	—	99	55
20	2·3	2·43	0·254	0·666	—	—	100	50
25	3·6	2·44	0·186	0·671	128	73	102	65

* Assuming the following to be adsorbed : A = $[Cr(PO_4)_2]^{6-}$; B = $[Cr(HPO_4)_2]^{3-}$; C = $[Cr(PO_4)_2]^{3-}$; D = $[Cr(HPO_4)_2]^-$ together with free phosphate.

(*b*) *From phosphoric acid solutions at 40° (100 ml.).*

Solutions : P_2O_5 (%)	1	5	10	15	20	25
Resin : Mol. of PO_4 adsorbed per equiv. of resin	0·651	0·660	0·642	0·641	0·655	0·647

Cation-exchange Experiments at 40°.—The results of similar experiments with the hydrogen form of the cation-exchanger Zeo-Karb 225 are given in Tables 6*a* and 6*b*. These results show an appreciable adsorption of phosphate (which varies with the time of contact of the resin with the solutions), thus indicating the presence of cationic phosphato-complexes.

TABLE 6. *Adsorption of chromium and phosphate by Zeo-Karb 225-H (0·500 g.) from chromic phosphate solutions at 40° (100 ml.).*

Solutions			Resin				
P_2O_5 (%)	$[PO_4]/[Cr]$	pH	Capacity (m. equiv./g.)	Mol. adsorbed/ equiv. of resin : Cr	PO_4	Capacity accounted for (%) * A	B
			(*a*) *After 10—14 days' contact with the resin.*				
1	16·4	1·54	3·30	0·368	0·157	79	95
5	8·6	1·18	3·54	0·281	0·022	80	82
10	5·0	1·00	3·58	0·285	0·037	78	82
15	2·8	1·04	3·64	0·372	0·161	79	96
20	2·3	1·10	3·58	0·430	0·288	71	101
25	3·6	0·62	3·59	0·367	0·275	55	83
			(*b*) *After 3—4 days' contact with the resin.*				
3	11·8	1·34	3·70	0·507	0·359	80	116
7·5	6·4	1·01	3·72	0·435	0·260	79	105
12·5	3·7	1·03	3·84	0·494	0·344	79	114

* Assuming the following to be adsorbed : A = $[Cr(HPO_4)]^+$ and B = $[Cr(H_2PO_4)]^{2+}$ or $[Cr(H_2PO_4)_2]^+$ together with $[Cr(H_2O)_6]^{3+}$ ions.

Discussion

Nature of the Solutions.—The ion-exchange studies at 0° (Tables 3 and 4) fail to show the presence of either anionic or cationic phosphato-complexes. This observation, taken in conjunction with the purple colour of the solutions, suggests that the chromium is present as the hexaquochromic ion, $[Cr(H_2O)_6]^{3+}$. At the higher concentrations the solutions became emerald-green after about 12 weeks, although solutions containing up to about 35% of phosphoric oxide were still purple after about 6 months. The change in colour of the more concentrated solutions would appear to be partially reversible since such solutions, on dilution, often rapidly reverted to their original purple colour. This could be due to the fact that only one of the co-ordinated water molecules is replaced by an $H_2PO_4^-$ group to give $[Cr(H_2O)_5(H_2PO_4)]^{2+}$. (Such a process would be favoured by the high concentration of $H_2PO_4^-$ ions in these solutions.) The view that the phosphato-group here acts as a monodentate group finds support in the fact that when it does occupy two co-ordination positions it is much more difficult to displace: thus the green solutions obtained at 40° do not revert to the purple form either on dilution or during long periods at 0° except in the presence of strong mineral acid (nitric or perchloric acid).

In the case of the green solutions at 40° the nature of the ions present in solution is not so clear. The results of the anion-exchange experiments (Table 5) have been calculated in terms of the capacity of the resin for various possible complexes in a fashion similar to that employed in the study of the aluminium phosphates (Jameson and Salmon, *J.*, 1954, 4013), and they would seem to imply that it is the $[Cr(PO_4)_2]^{3-}$ ion that is adsorbed. In this respect it is of interest that the ratio of phosphate to chromium in stable solutions reaches a minimum value approaching two (Table 2) as compared with a value of three for the corresponding ratio in the ferric phosphate system (Jameson and Salmon, *J.*, 1954, 28) where the complex is a triphosphato one. The corresponding minimum is also three for the aluminium phosphate system (Jameson and Salmon, *J.*, 1954, 4013), but barely reaches a value of four in the chromic phosphate system at 0° (Table 1) where no phosphato-complexes are formed and the salts are those of a relatively weak base and a fairly strong acid. {If the minimum value of the ratio of phosphate to chromium has the significance just implied then the concentration of cationic complexes of the type $[Cr(HPO_4)]^+$ (see below) must be very low.}

Care is needed in the interpretation of the results of the cation-exchange experiments at 40° since the adsorption of the cationic complexes is marked by several unusual features. Thus, not only is the adsorbed material difficult to remove (requiring 3—4N-acid), but the time of contact of the resin with the solution appears to affect the adsorption (Table 6), and in addition the time for which the solutions are aged is probably a significant factor. The results of the experiments at 0° seem to suggest that the size of the hexaquochromic ion prevents its occupying all the available exchange sites of the resin and, if this is the case, then any ion containing both co-ordinated water and phosphato-groups would be expected to lead to this low effective capacity to an even greater extent. The constant (low) effective capacity for the $[Cr(HPO_4)]^+$ ion (Table 6) (it remains constant whatever the time of contact of the solution with the resin) suggests, therefore, that this is the ion initially adsorbed—the results obtained with a short time of contact between resin and solution appear to exclude the adsorption of both $[Cr(H_2PO_4)]^{2+}$ and $[Cr(H_2PO_4)_2]^+$ (at least in major amount). Subsequently, under the influence of the resin (*e.g.*, by acid catalysis by the sulphonic acid groups), a change in the species adsorbed occurs to give the hexaquochromic ion, possibly by means of a reaction of the type:

$$\overline{3[Cr(HPO_4)]^+} + H_3PO_4 \longrightarrow \overline{Cr^{3+}} + 2[Cr(HPO_4)(H_3PO_4)]$$

(where barred formulæ indicate the resin phase)

[Gustavson (*Svensk Kem. Tidskr.*, 1951, **63**, 167) has in fact reported that the functional groups of a cation-exchanger may act as ligand groups and even displace other groups originally bound in the complex.]

The minimum in the amount of chromium adsorbed by the anion-exchanger that is exhibited at about 7½% of phosphoric oxide in the solutions is presumably a concentration

effect, since at this point the chromium content of the solutions is beginning to increase rapidly as the ratio of phosphate to chromium is decreasing (Tables 2 and 5), which factors might hinder the formation of anionic complexes. In the cation-exchange experiments (Table 6) it is not clear whether the similar dip in the adsorption of phosphate would persist with even shorter time of contact with the resin. In both cases the ageing of the solutions may well play a part.

Heating the solutions to temperatures much in excess of 40° seems to change markedly the nature of the ions present in solution. The solutions become uncrystallizable (Vauquelin, *Ann. Chim. Phys.*, 1798, **25**, 194) and have only a very small concentration of adsorbable anionic and cationic complexes (Holroyd and Salmon, unpublished work). In the present work, therefore, none of the solutions was heated above 40°.

Nature of the Solid Phases.—Very little can be said as to the nature of the solids without *X*-ray or similar examination. The purple solids presumablyc ontain the hexaquochromic ion and phosphate ions, *e.g.*, the compound $2Cr_2O_3,3P_2O_5,51H_2O$ would be $[Cr(H_2O)_6]_2[HPO_4]_3,12H_2O$—although in this case the water content may be variable (and possibly zeolitic in nature).

In the green compounds at 40° the compound $Cr_2O_3,3P_2O_5,10H_2O$ is most probably $H_3[Cr(HPO_4)_3],2H_2O$, although no evidence for the triphosphato-ion is found in the range of solutions containing up to 25% of phosphoric oxide. From the anion-exchange experiments at 40° (Table 5), the compound $Cr_2O_3,2P_2O_5,8H_2O$ could quite well be $H_3[Cr(PO_4)_2(H_2O)_2],\frac{1}{2}H_2O$, and $Cr_2O_3,P_2O_5,12H_2O$ may be $[Cr(H_2O)_6][Cr(PO_4)_2(H_2O)_2],4H_2O$.

Experimental

Apparatus.—For the experiments at both 0° and 40° air thermostats were used. The samples were contained in "Pyrex" boiling-tubes closed with rubber bungs or with glass stoppers and held in a lagged box within the thermostats; the temperature variation was less than 0·1°.

Preparation of Solutions.—The solutions were prepared by dissolving the purple tertiary salt in solutions of phosphoric acid. This gave rise to deep purple solutions which, on being kept at 0°, deposited crystals and reached a state of equilibrium after about 6—8 weeks. The solutions could easily be supersaturated by warming them to 30° for a short time and dissolving the solid at this temperature before cooling them rapidly to 0°.

In the study of the system at 40° it seemed desirable (for the reasons given above) to avoid warming the solutions above this temperature. The solutions were therefore maintained at 40° and kept well stirred, more solid being added when necessary, until a supersaturated solution had been attained which would then crystallize out.

At both 0° and 40° the method of analysing alternate tubes in any given batch of 12 was employed. Two weeks were allowed to elapse between the analysis of the first and the second sets of solutions (and solids), and a smooth solubility isotherm was taken as a criterion of equilibrium. The time taken to reach equilibrium ranged from 6 to 10 weeks.

Preparation of the Purple Tertiary Chromic Phosphate.—Because of its nicely crystalline nature which made possible its preparation in a pure state, the compound used as starting material in all the present work was the purple tertiary salt, $[Cr(H_2O)_6]PO_4$, which was prepared as follows: "AnalaR" chromium potassium sulphate (120 g.) was dissolved in distilled water (1·5 l.). A solution of "AnalaR" disodium hydrogen phosphate (30 g.) was then added dropwise with continual (mechanical) stirring of the liquid. Immediately following this a solution of ammonium acetate (30 g.) in water (500 ml.) was added dropwise and the stirring continued for another 2 hr. The precipitate was washed several times by decantation and, finally, on a Büchner funnel, with cold water. A lavender-coloured solid (about 60 g.) was obtained; the product was nicely crystalline (small hexagonal plates) and gave no flame-test for sodium. Analysis of a typical batch of the air-dried material gave: Cr_2O_3, 29·74; P_2O_5, 27·74; H_2O, 42·50% (Calc. for $Cr_2O_3,P_2O_5,12H_2O$: Cr_2O_3, 29·80; P_2O_5, 27·83; H_2O, 42·37%).

Resins.—The strongly acidic, monofunctional cation-exchanger Permutit Zeo-Karb 225 and the strongly basic, monofunctional anion-exchanger Amberlite I.R.A.-400 were used. The former was in the hydrogen form and the latter in the form of its phosphate to avoid the introduction of foreign ions into the solutions on exchange. The resin used for the separation of chromium from phosphate in the case of the purple (*i.e.*, complex-free) solids and solutions was Permutit Zeo-Karb 215, a cation-exchanger having both phenolic and sulphonic acid groups as the active centres.

The technique was that previously employed for the study of the aluminium phosphates (Jameson and Salmon, *J.*, 1954, 4013) except that in elution of the species adsorbed at 40° 3—4N-nitric acid had to be used in place of 2N-nitric acid.

Analytical Methods.—Chromium was determined, after oxidation to dichromate, by addition of a standard ferrous ammonium sulphate solution, followed by back-titration of the excess with standard potassium dichromate solution.

Phosphate, in the case of the purple (*i.e.*, complex-free) system, was estimated by titration with standard bismuthyl perchlorate solution (M/20 approx.) with thiourea as indicator (Salmon and Terrey, *J.*, 1950, 2813) after removal of chromium by percolation of the solution through a column of Permutit Zeo-Karb 215 in the hydrogen form; perchloric acid was used to dissolve the solids and to stabilize the solutions.

The stable complexes present in the green solutions prevented the use of ion-exchange resins to effect the removal of chromium from these solutions and so the phosphate was precipitated from them as ammonium phosphomolydate, dried at 115°, and weighed. This procedure was adopted universally for small amounts of phosphate; perchlorates do not interfere.

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Ferrocene Derivatives. Part II. Arylation.*

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It is shown that aryl groups may be introduced into ferrocene by reaction with diazonium salts or with nitrosoacetanilide.

FERROCENE can be obtained by the reaction of *cyclo*pentadienylmagnesium bromide (or of the alkali-metal derivatives of *cyclo*pentadiene) with ferric chloride (Kealy and Pauson, *Nature*, 1951, **168**, 1039). In Part I * of this series, this method was extended to the preparation of di-, tetra-, and hexa-phenylferrocene from the corresponding phenyl-substituted *cyclo*pentadienes. It was also shown that a small yield of monophenylferrocene can be obtained by using a mixture of *cyclo*pentadiene and phenyl*cyclo*pentadiene. The inaccessibility of phenyl*cyclo*pentadiene, however, made this route impracticable on a larger scale. We now describe a reaction which makes mono- and di-phenylferrocene readily accessible and can be extended to other arylferrocenes.

Although ferrocene undergoes smooth Friedel–Crafts acylation (Woodward, Rosenblum, and Whiting, *J. Amer. Chem. Soc.*, 1952, **74**, 3458), other typical aromatic substitution reactions have been limited by the ease of oxidation of ferrocene to metalation with *n*-butyl-lithium (Benkeser, Goggin, and Schroll, *ibid.*, 1954, **76**, 4025). We have found that ferrocene is readily arylated on treatment with diazonium salts.† Adding benzenediazonium sulphate solution to approx. 1 mol. of ferrocene in glacial acetic acid causes steady evolution of gas during several hours at 0°. On chromatography of the product some ferrocene is always recovered. Allowing for this, a 65% yield of phenylferrocene (approx. 40% conversion) is obtained together with 9% of diphenylferrocene. A similar reaction occurred in acetone. By the use of other diazonium salts, *p*-methoxy-, *o*-methyl-, and *m*-chlorophenylferrocene were readily isolated in 35—45% yields. We have also applied the reaction with success to diazotised *p*-hydroxyaniline, anthranilic acid, and sulphanilic acid.

The only limitation of the reaction is again due to the ease of oxidation of ferrocene and was encountered with 2 : 4-dinitroaniline; a considerable proportion of the ferrocene was converted into ferricinium salt, and the diazonium salt reduced to *m*-dinitrobenzene.

* Part I, *J. Amer. Chem. Soc.*, 1954, **76**, 2187.

† [Added 12.12.54.] An example of this reaction has recently been reported (Nesmeyanov, Perevalova, Golovnya, and Nesmeyanova, *Doklady Akad. Nauk S.S.S.R.*, 1954, **97**, 459), and ferricinium salts have been shown to undergo similar reactions (Weinmayr, *J. Amer. Chem. Soc.*, in the press).

Only in one experiment were we able to isolate a few dark purple crystals believed to consist of 2 : 4-dinitrophenylferrocene, but the amount was insufficient for complete characterization.

Intermediate behaviour was shown by *o*- and *p*-nitrobenzenediazonium salts. The expected nitrophenylferrocenes were readily isolated, but the yields were rather low and a strong smell of nitrobenzene together with the presence of much ferricinium salt indicated oxidation–reduction.

Disubstitution products are undoubtedly always formed in small yield, but we have isolated these only in a few representative cases. It is, however, clear from these that the second substituent enters preferentially the unsubstituted ring to yield the 1 : 1′-diarylferrocene. In the case of di-(*p*-methoxyphenyl)ferrocene a second isomer is readily isolated from the chromatogram although in much smaller yield. That this has one unsubstituted *cyclo*pentadiene ring is indicated by the presence of characteristic bands in the infra-red spectrum (cf. Part I, *loc. cit.*), but it is unknown whether the second aryl group has entered at position 2 or 3 or into the first aryl group.

The diphenylferrocene fraction appeared chromatographically homogeneous and the recrystallized product was identical with the product described in Part I (*loc. cit.*). However, the material from the chromatogram was low-melting and the mother liquors from the recrystallizations gave a viscous oil, the infra-red spectrum of which showed bands characteristic of ferrocene derivatives with one unsubstituted ring.

To obtain larger amounts of diphenylferrocene, benzenediazonium sulphate was allowed to react with phenylferrocene, a 52% yield (26% conversion) being obtained together with a small amount of a triphenylferrocene of unknown orientation.

The arylation of ferrocene here described is reminiscent of the free-radical arylations studied chiefly by Gomberg and Hey and their collaborators, but our conditions differ sufficiently from those of a normal Gomberg reaction to raise doubts whether aryl radicals are involved in this case. To obtain further evidence the reaction conditions were varied. When ferrocene reacted in *cyclo*hexane with the benzenediazonium chloride–zinc chloride complex or with *N*-nitrosoacetanilide, mono- and di-phenylferrocene were obtained in yields and proportions similar to those obtained in acetic acid. On the other hand ferrocene was not attacked by phenylazotriphenylmethane in warm *cyclo*hexane or by phenyl radicals generated from a mixture of phenylmagnesium bromide and bromobenzene by cobaltous chloride or (cf. Part I) by benzoyl peroxide. It is considered probable that ferrocene and the diazonium salt form an intermediate complex which rearranges to give the observed products either directly, or *via* a ferricinium salt as suggested by the experiment in which acetone was used as solvent (see p. 369). A more detailed study is in progress.

Experimental

Light petroleum used had b. p. 40—60°.

General Method.—A solution of the appropriate diazonium chloride or sulphate was prepared in the conventional manner in as small a volume of water as convenient. This solution was rapidly dropped into a stirred solution of ferrocene (3 g.) in glacial acetic acid (100 ml.) at room temperature, under nitrogen. At the end of the reaction (which may conveniently be ascertained by testing a small sample of the mixture with alkaline β-naphthol) or next morning, water was added, followed by sufficient titanous sulphate solution to reduce any ferricinium salt present. The whole was then extracted with ether, washed with water and sodium carbonate solution, dried (Na_2SO_4), and evaporated. The residue was chromatographed on activated alumina, except in the case of the carboxylic and sulphonic acids.

Yields are based on unrecovered ferrocene.

Mono- and Di-phenylferrocene.—(*a*) Benzenediazonium sulphate prepared from aniline (1·5 ml.) was used. Light petroleum (b. p. 40—60°) was employed throughout the chromatographic separation. In a typical run 41% of ferrocene was recovered and, after allowance for this, the yields of mono- and di-phenylferrocene were 66% and 9% respectively. Both products after crystallization from light petroleum had m. p.s identical with and undepressed by those of the products described in Part I (*loc. cit.*). In larger-scale experiments ferrocene was removed from the products by steam-distillation before the chromatographic separation.

(*b*) With acetone in place of acetic acid, ferrocene yielded an immediate greenish-blue precipitate (presumably a ferricinium salt) on addition of aqueous benzenediazonium sulphate. Brisk evolution of nitrogen soon commenced and next morning the precipitate had completely redissolved. The clear brown solution yielded unchanged ferrocene (37%) and phenylferrocene (36%) together with small amounts of higher substitution products.

(*c*) The benzenediazonium chloride–zinc chloride double salt (Hodgson and Marsden, *J.*, 1940, 208) (3·7 g.), sodium acetate (0·6 g.), and glacial acetic acid (0·62 g.) were added to a stirred solution of ferrocene (3 g.) in *cyclo*hexane (100 ml.) under nitrogen. After being kept overnight, the mixture was worked up as before, yielding phenylferrocene (33%) and diphenylferrocene (9%), after recovery of ferrocene (32%).

(*d*) *N*-Nitrosoacetanilide (2·64 g.) was rapidly added to the stirred solution of ferrocene (3 g.) in *cyclo*hexane (100 ml.). The mixture was warmed to 50° to initiate the reaction and then kept at room temperature overnight. Working up as before gave ferrocene (54%) and mono- (46%) and di-phenylferrocene (8%).

Attempted Reaction of Ferrocene with Phenylazotriphenylmethane.—Phenylazotriphenylmethane (3·6 g.) was added to a solution of ferrocene (2 g.) in *cyclo*hexane. The mixture was heated at 50—60° for 2 hr. and then at the boiling point until nitrogen evolution ceased. On evaporation and chromatography ferrocene was recovered almost quantitatively.

Further Phenylation of Phenylferrocene.—Phenylferrocene (5 g.) in acetic acid (150 ml.) was allowed to react with the diazonium sulphate prepared from aniline (2·13 g.). Light petroleum was employed for chromatography and separated unchanged phenylferrocene (49%) from diphenylferrocene (52%) and *triphenylferrocene* (10%), which crystallized from light petroleum as an orange powder, m. p. 116—118° (Found: C, 80·6; H, 5·7. $C_{28}H_{22}Fe$ requires C, 81·2; H, 5·4%).

o-*Tolylferrocene.*—The diazonium chloride prepared from *o*-toluidine (1·72 g.) was used. A mixture of light petroleum and *cyclo*hexane effected chromatographic separation of the product from unchanged ferrocene (31%) and a small amount of ditolylferrocene (not isolated pure). o-*Tolylferrocene* (43%) crystallized from alcohol in orange leaflets, m. p. 51—52° (Found: C, 73·6; H, 6·0. $C_{17}H_{16}Fe$ requires C, 73·9; H, 5·8%).

m-*Chlorophenyl- and Di*-m-*chlorophenyl-ferrocene.*—The diazonium chloride was prepared from *m*-chloroaniline (2·1 g.). Light petroleum was used for chromatography. The first band consisted of unchanged ferrocene (30%). The second band yielded m-*chlorophenylferrocene* (34%) crystallizing from light petroleum in orange leaflets, m. p. 77—78° (Found: C, 64·7; H, 4·6. $C_{16}H_{13}ClFe$ requires C, 64·8; H, 4·5%). The final band afforded 1 : 1′-*di*-m-*chlorophenylferrocene* (0·4%), obtained as a microcrystalline powder, m. p. 183—184° from *cyclo*hexane (Found: C, 64·9; H, 4·0. $C_{22}H_{16}Cl_2Fe$ requires C, 64·9; H, 4·0%).

p-*Methoxyphenyl- and Di*-p-*methoxyphenyl-ferrocene.*—The diazonium chloride was prepared from *p*-anisidine (2 g.). A mixture of *cyclo*hexane and benzene was employed for chromatography, yielding ferrocene (54%) followed by p-*methoxyphenylferrocene* (35%), crystallizing from *cyclo*hexane as orange-yellow leaflets, m. p. 112—114° (Found: C, 70·25; H, 5·6. $C_{17}H_{16}OFe$ requires C, 69·9; H, 5·5%). 1 : 1′-*Di*-p-*methoxyphenylferrocene* (7%), crystallizing from the same solvent as orange leaflets, m. p. 167—168° (Found: C, 72·4; H, 5·4. $C_{24}H_{22}O_2Fe$ requires C, 72·4; H, 5·6%), was isolated from the last (fourth) band of the chromatogram. An *isomer* (0·7 %) forming dark orange crystals from *cyclo*hexane, m. p. 112—114° (depressed to 90° on admixture with the monosubstitution product) was isolated from the intermediate (third) fraction (Found: C, 72·4; H, 5·7%).

p-*Hydroxyphenylferrocene.*—The diazonium chloride was prepared from *p*-aminophenol (4·7 g.). The product was strongly adsorbed on alumina and, after removal of unchanged ferrocene (20%) by benzene, was extracted by boiling the adsorbent with alcohol. p-*Hydroxyphenylferrocene* (14%) crystallized from absolute alcohol in orange-yellow leaflets, m. p. 163—164° (Found: C, 68·9; H, 5·3%. $C_{16}H_{14}OFe$ requires C, 69·1; H, 5·1%).

o-*Carboxyphenylferrocene.*—The diazonium chloride was prepared from anthranilic acid (2·2 g.). The ethereal solution of the products was extracted with 2N-sodium hydroxide. The neutral fraction gave ferrocene (66%). Acidification of the alkaline solution precipitated o-*carboxyphenylferrocene* (7%) which crystallized from light petroleum in orange needles, m. p. 128—129° (Found: C, 66·7; H, 4·7. $C_{17}H_{14}O_2Fe$ requires C, 66·7; H, 4·6%).

Barium p-*Ferrocenylbenzenesulphonate.*—The diazonium chloride prepared from sulphanilic acid (3·36 g.) was added to the ferrocene solution. After 12 hr. the mixture was diluted with water, titanous chloride added, and the precipitated ferrocene filtered off. Addition of aqueous barium chloride solution to the filtrate precipitated *barium* p-*ferrocenylbenzenesulphonate* as an

orange-brown powder. It was recrystallized from water (Found: C, 41·0; H, 4·1; S, 7·15. $C_{32}H_{36}O_6S_2BaFe_2,6H_2O$ requires C, 40·7; H, 4·05; S, 6·8%. $C_{32}H_{36}O_6S_2BaFe_2,5H_2O$ requires C, 41·5; H, 3·9; S, 6·9%).

o-Nitrophenylferrocene.—The diazonium chloride was prepared from *o*-nitraniline (4·46 g.). Chromatography with a mixture of *cyclo*hexane and benzene separated unchanged ferrocene (23%) from *o-nitrophenylferrocene* (5%), which crystallized from light petroleum in purple plates, m. p. 112—114° (Found: C, 61·8, 63·1; H, 4·2, 4·7; N, 4·3. $C_{16}H_{13}O_2NFe$ requires C, 62·6; H, 4·3; N, 4·6%).

p-Nitrophenylferrocene.—The diazonium chloride was prepared from *p*-nitroaniline (4·46 g.). The chromatogram was developed with benzene–ether, separating unchanged ferrocene (20%) from *p-nitrophenylferrocene* (18%) which formed deep purple rhombs (from absolute alcohol), m. p. 169—170° (Found: C, 62·2; H, 4·35; N, 4·9%).

Reaction of Ferrocene with Diazotized 2 : 4-Dinitroaniline.—An acetic acid solution of the diazonium sulphate from 2 : 4-dinitroaniline (3 g.) was used. Chromatography of the products with benzene yielded ferrocene (40%) followed on the column by *m*-dinitrobenzene. The latter was always contaminated by a trace of purple material, but in only one experiment out of three could a few dark purple crystals be separated from the mother-liquors after crystallization of this fraction.

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The Oppenauer Oxidation of Ergocalciferol.

By S. TRIPPETT.

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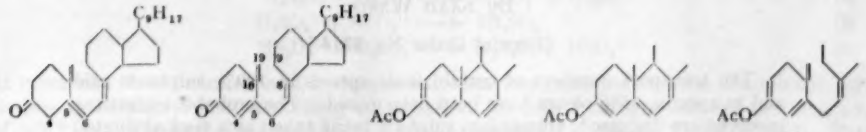
Oppenauer oxidation of ergocalciferol gave the crystalline conjugated ketone (II), which is reduced by lithium aluminium hydride or the Meerwein–Pondorf method without rearrangement. Attempts to convert the ketone into ergocalciferol *via* an enol acetate, or by treatment with *tert.*-butyl chloride followed by sodium borohydride, failed.

BY Oppenauer oxidation of ergocalciferol, Windaus and Buchholz (*Z. physiol. Chem.*, 1938, **256**, 273) obtained a non-crystalline ketone thought to have the structure (I) or (II), which had maximum light absorption in ethanol at 265 mμ and gave a semicarbazone with a maximum in chloroform at 293 mμ. They stated that Meerwein–Pondorf reduction of the ketone, purified by regeneration from its semicarbazone, gave ergocalciferol, isolated as the 3 : 5-dinitrobenzoate in 5·3% yield. Both the absolute value of the absorption maximum of the semicarbazone, and its difference from that of the ketone, suggest the αβ-unsaturated structure (II) rather than (I); if this were the case, the regeneration of ergocalciferol on reduction must be accompanied by a migration of the double bond from the 4 : 5 to the 5 : 6-position. Similar migrations have been recorded for steroids containing an intact ring B (for summary see Wilds, "Organic Reactions," J. Wiley & Son Inc., New York, 1944, Vol. II, p. 178), but this appears to be the sole example of a migration to an exocyclic position, so the original work was repeated.

Oppenauer oxidation of ergocalciferol, with acetone as the hydrogen acceptor, gave a crystalline ketone with maximum light absorption in ethanol at 272 mμ. The semicarbazone had $\lambda_{max.}$ 293 mμ in chloroform. The infra-red spectrum of the ketone showed bands at 1678 and 1590 cm.$^{-1}$ in "Nujol" suspension, as required by the conjugated ketone structure (II). The crude oxidation product gave the same semicarbazone and was free from absorption bands in the infra-red near 1720 cm.$^{-1}$, showing the absence of unrearranged ketone (I). According to Windaus and Buchholz (*loc. cit.*), the ketone (II) could be regenerated from its semicarbazone by the action of benzaldehyde in 80% ethanol under reflux,

but this was found to be possible only if benzaldehyde containing benzoic acid was used, and even then the product was difficult to purify. However, regeneration with pyruvic acid gave the original ketone in good yield. Meerwein–Pondorf or lithium aluminium hydride reduction of the ketone (II) gave a syrupy alcohol having maximum light absorption in ethanol at 235 mμ in agreement with the maximum at 237 mμ calculated for the alcohol derived from (II). The alcohol showed no selective light absorption at 265 mμ and this, and its failure to give a crystalline **3** : 5-dinitrobenzoate, shows that it contained no ergocalciferol.

Attempts were then made to convert the ketone (II) into ergocalciferol *via* the enol acetate (for the conversion of cholest-4-en-3-one into cholesterol *via* the enol acetate see Belleau and Gallagher, *J. Amer. Chem. Soc.*, 1951, **73**, 4458). Acetylation with acetic



(I) (II) (III) (IV) (V)

anhydride and pyridine gave an enol acetate having maximum light absorption in ethanol at 306 mμ. Of the two enol acetates of cholest-4 : 6-dien-3-one, 3-acetoxy-cholesta-2 : 4 : 6-triene (III) has maximum light absorption in ethanol at 302 mμ and 3-acetoxycholest-3 : 5 : 7-triene (IV) at 316 mμ (Dauben, Eastham, and Micheli, *ibid.*, 1951, **73**, 4496); the enol acetate obtained from (II) is therefore formulated as the 3-acetoxy-2 : 4 : 7 : 10(19)-tetraene (V). In agreement with this, reduction with sodium borohydride gave no ergocalciferol. Acetylation of the ketone (II) under acidic conditions, *e.g.*, with acetyl chloride and acetic anhydride, caused migration of the exocyclic methylene double bond. Treatment of the ketone (II) with *tert.*-butylmagnesium chloride, followed by reduction with sodium borohydride, gave a product which, from its light absorption, contained no ergocalciferol.

Experimental

Oppenauer Oxidation of Ergocalciferol.—Ergocalciferol (4·2 g.) and aluminium *tert.*-butoxide (5 g.) were boiled in dry benzene (500 c.c.) and acetone (150 c.c.) under reflux in an atmosphere of nitrogen for 16 hr. After dilution with water, evaporation of the benzene layer gave a product containing much mesityl oxide. This was removed under reduced pressure and the residue crystallised from light petroleum (b. p. 40—60°) at −40° to give 9 : 10-seco*ergosta*-4 : 7 : 10(19) : 22-*tetraen*-3-*one*, m. p. 72—73°, $[\alpha]_D$ +37·5° (*c*, 2·6 in $CHCl_3$), $\lambda_{max.}$ 272 mμ (ε 14,600 in EtOH) (Found: C, 84·9; H, 10·9. $C_{28}H_{42}O$ requires C, 85·2; H, 10·7%). The semicarbazone, prepared from the crude oxidation product or from crystalline ketone, at room temperature or under reflux (cf. Windaus and Buchholz, *loc. cit.*), and crystallised from methanol–chloroform, had m. p. 217—218° (decomp.), $\lambda_{max.}$ 293 mμ (ε 31,300 in $CHCl_3$) (Found: N, 9·4. Calc. for $C_{29}H_{45}ON_3$: N, 9·3%).

The semicarbazone (0·62 g.) in acetic acid (10 c.c.) and water (2 c.c.) was heated on the steam-bath with pyruvic acid (2 c.c.) for 15 min. After addition of water, extraction with ether gave a product which crystallised from light petroleum (b. p. 40—60°) to give the ketone (II) (0·42 g.), m. p. and mixed m. p. 72—73°.

The ketone (II) (0·2 g.), when heated under reflux with pyridine (2 c.c.) and acetic anhydride (0·5 c.c.) for 3 hr., gave the *enol acetate* (V), b. p. 150° (bath-temp.)/10^{-4} mm., $\lambda_{max.}$ 306 mμ (ε 21,900 in EtOH), $\nu_{max.}$ 1751, 878 cm.$^{-1}$ (Found: C, 82·8; H, 10·5. $C_{30}H_{44}O_2$ requires C, 82·5; H, 10·2%).

Meerwein–Pondorf Reduction of the Ketone (II).—The ketone (0·31 g.) and aluminium *iso*propoxide (1 g.) were heated in dry *iso*propanol (100 c.c.) under reflux in an atmosphere of nitrogen for 9 hr. with continuous slow removal of *iso*propanol. After dilution with water, ether-extraction gave the *alcohol* as a colourless syrup, $\lambda_{max.}$ 235 mμ (ε 14,700 in EtOH), $\nu_{max.}$ 3300, 1608, 970, 880 cm.$^{-1}$ (Found: C, 84·8; H, 11·6. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%). From the absolute intensity of the light absorption of the alcohol at 265 mμ, there could not be more than 3% of ergocalciferol present, and the smooth shape of the curve at this point made

even this improbable. A similar reduction of the crude ketone, obtained by regeneration from the semicarbazone with pyruvic acid, again gave a product containing no ergocalciferol. This eliminated the possibility that a small amount of the unconjugated ketone (I) might have been formed during the regeneration.

The author thanks Professor B. Lythgoe for his interest and advice.

THE UNIVERSITY, LEEDS, 2. [*Received, October 18th*, 1954.]

Properties of Sulphuric Acid Solutions. Part I. Transport-number Measurements in Sulphuric Acid and Oleum Solutions.

By SAAD WASIF.

[Reprint Order No. 5314.]

The transport numbers of certain ionic species in 100% sulphuric acid and in approx. 35% oleum have been determined. The probable ionisations involved are discussed, ammonium sulphate being taken as a typical solute.

THE purpose of this work is to extend the study of electrical conductivity in absolute sulphuric acid and in oleum solutions (Gillespie and Wasif, *J.*, 1953, 204, 209, 215, 221, 964). The transport numbers of some new ions, chiefly ammonium sulphate, acetic acid, and benzoic acid, have been measured in absolute sulphuric acid. Another series of transport-number measurements of these solutes and of alkali and alkaline-earth cations was carried out in oleum solutions (~35% SO_3).

EXPERIMENTAL

All the measurements were carried out by Hittorf's method at 25°, solutions of known concentrations of the different solutes being prepared and analysed before electrolysis.

Ammonium sulphate was determined by adding excess of ~30% sodium hydroxide solution to the solution in sulphuric acid, and estimation of the evolved ammonia in the usual manner.

For determination of acetic acid, the sulphuric acid was titrated by sodium carbonate until the solution contained only sodium hydrogen sulphate and acetic acid. Acetic acid was distilled off under a partial vacuum (~26 mm.) into a known volume of standard alkali, the excess of which was then titrated by standard hydrochloric acid. The following Table * contains the transport numbers found for some ions in sulphuric acid (A) and in 15% oleum (B).

DISCUSSION

The foregoing results show that the general nature of ionic transport and electrical conductivity was somewhat similar in sulphuric acid and in oleum. However, owing to certain differences in the nature and composition of such solutions, they are discussed separately.

Ion	*m*	Amount of electricity passing (c)	$10^5 \times$ Increase in cathode concn.	$10^5 \times$ Decrease in anode concn.	Transport number : cation	anion
$CH_3{\cdot}CO_2H_2^+$ ...	0·5723 (A)	6523	150	151·6	0·022	0·0224
NH_4^+	0·4766 (A)	5910	189·7	183·6	0·031	0·030
	0·7836 (A)	5423	202·3	174·2	0·036	0·031
	0·9780 (A)	5885	207·4	244	0·034	0·040
Na^+	0·2240 (B)	2355	42	42	0·017	0·017
$\frac{1}{2}Sr^{++}$	0·2546 (B)	3416	77·8	42·5	0·022	0·012
$\frac{1}{2}Ba^{++}$	0·5060 (B)	4834	60·1	50·1	0·012	0·01
$CH_3{\cdot}CO_2H_2^+$ ...	0·3521 (B)	3917	251	250	0·061	0·061
NH_4^+	0·5629 (B)	5790	21	186	0·035	0·031
K^+	0·4600 (B)	3860	116	132	0·029	0·033

* *m* = Molality of solute (mole per kg. of sulphuric acid or oleum); other concentrations are given in g.-equiv. per kg. of solvent.

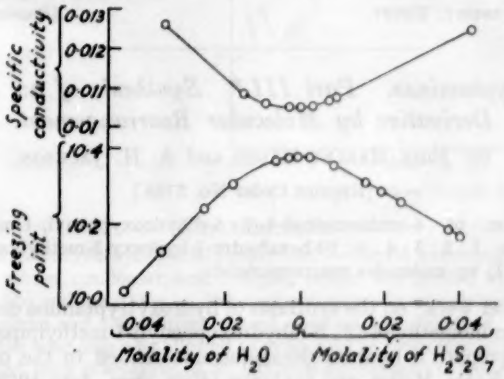
(1) *Conductivities in Absolute Sulphuric Acid Solutions.*—The transport-number data of acetic acid, benzoic acid, and ammonium sulphate suggest that the hydrogen sulphate ion

conducts most of the current (97—99%) and most probably by the abnormal mechanism suggested earlier (*J.*, 1953, 209). It is noteworthy, however, that the transport numbers of the NH_4^+ ion did not change much with concentration. This is not in accord with the results obtained from Ba^{++} and Sr^{++} which were explained by the assumption that the high viscosity of their solutions made ionic diffusion more difficult (*loc. cit.*).

(2) *Conductivities in Oleum Solutions* (*Conduction of the Ion*, $H_3SO_4^+$, *in Oleum*).—The Table contains the results of the transport-number measurements of some solutes in oleum solutions of nearly the same sulphur trioxide concentration (~15%). In such solutions solutes are ionised according to a scheme for which we may take ammonium sulphate as an example:

$$(NH_4)_2SO_4 + H_2SO_4 \longrightarrow 2NH_4^+ + 2HSO_4^- \quad (1)$$
$$H_2S_2O_7 + H_2SO_4 \longrightarrow H_3SO_4^+ + HS_2O_7^- \quad (2)$$
$$H_3SO_4^+ + HSO_4^- \longrightarrow 2H_2SO_4 \quad (3)$$
$$HS_2O_7^- + H_2SO_4 \longrightarrow H_2S_2O_7 + HSO_4^- \quad (4)$$

It gives rise to ammonium and hydrogen sulphate ions, and part of the disulphuric acid ionises in sulphuric acid according to equation (2) into hydrogen disulphate ions and $H_3SO_4^+$ ions. The latter ions react according to equation (3) (Gillespie, *J.*, 1950, 2542). Part



of the hydrogen disulphate ions will, however, be solvolysed by sulphuric acid (4) to give rise to hydrogen sulphate ions. In such solutions we find that the NH_4^+ and $H_3SO_4^+$ ions are the only positive ions present and the $HS_2O_7^-$ and HSO_4^- ions are the corresponding negative ions. The amount of hydrogen sulphate ions could be calculated from a knowledge of the solvolysis constant of the hydrogen disulphate ion in sulphuric acid (*idem*, *ibid.*).

It should be pointed out that the amount of the hydrogen sulphate ions, however little it may be, will cause some error in the results in the Table, but this is not very serious because only about 30% of the disulphuric acid molecules are ionised, and only about 5—10% of the hydrogen disulphate ions are solvolysed according to equation (4) (*loc. cit.*). The amount of chain conduction due to the presence of hydrogen sulphate ions could not be more than 10% of the total chain conduction that would take place in such solutions. The results in the Table are therefore only approximate for these and other reasons. The other ions present are NH_4^+ and $HS_2O_7^-$, which have been shown (Gillespie and Wasif, *J.*, 1953, 209, 964) to carry only a small part of the current. The NH_4^+ ion in pure sulphuric acid was shown to carry only about 3% of the total current by the diffusion mechanism (see Table).

There is some doubt as to the nature of conduction of the hydrogen disulphate ion in these solutions. It is not certain that the chain mechanism would be the only way in which conduction takes place on account of the difficulty with which the proton would jump between the $HS_2O_7^-$ ion and H_2SO_4 molecules owing to the high potential barrier between the two entities (Glasstone, Laidler, and Eyring, "The Theory of Rate Processes,"

Van Nostrand, 1941). The conductivity of the hydrogen disulphate ion has been found not to exceed 5% of that of the hydrogen sulphate ion (Gillespie and Wasif, *J.*, 1953, 964).

The above considerations suggest that in such solutions the $H_3SO_4^+$ ion must be the one responsible for the process of chain conduction in oleum solutions in just the same way as the HSO_4^- ion conducts in pure sulphuric acid solutions. That such an ion conducts by an abnormal rather than the normal mechanism can be seen from the values of the transport numbers for the different ions measured in these solutions, and their comparison with those in absolute sulphuric acid. The mobility of the hydrogen ion was found to be comparable with that of the hydrogen sulphate ion from a consideration of the conductivity titration curve of the sulphur trioxide–water system and its comparison with the freezing-point curve for the same system (see Fig.). The maximum point on the f. p. curve, which was found to correspond to the composition of pure sulphuric acid, coincides with the minimum conductivity on the specific-conductivity curve. If the mobilities of the $H_3SO_4^+$ and the HSO_4^- ion were different, that would lead to a shift of the minimum point on the specific-conductivity curve towards the water side or towards the sulphur trioxide side according as the HSO_4^+ is the faster or the slower ion.

The author thanks Dr. R. J. Gillespie for his useful suggestions and continuous encouragement.

ALEXANDRIA UNIVERSITY, EGYPT. [*Received, April 5th,* 1954.]

Hydroxytryptamines. Part III. Synthesis of an Azepindole Derivative by Molecular Rearrangement.*

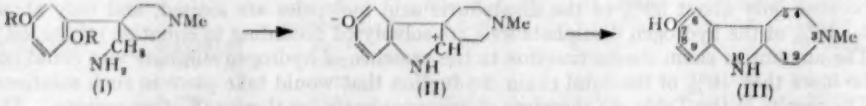
By JOHN HARLEY-MASON and A. H. JACKSON.

[Reprint Order No. 5748.]

Oxidation of 4-aminomethyl-4-(2 : 5-dihydroxyphenyl)-1-methylpiperidine gives 1 : 2 : 3 : 4 : 5 : 10-hexahydro-7-hydroxy-3-methylazep[4, 5-*b*]-indole † (III) by molecular rearrangement.

IN extension of earlier work* on the synthesis of hydroxytryptamine derivatives of physiological interest, 4-aminomethyl-4-(2 : 5-dihydroxyphenyl)-1-methylpiperidine was oxidised in an attempt to prepare a hydroxy*spiro*indolenine related to the oxindole derivatives obtained earlier by Kretz, Müller, and Schlittler (*Helv. chim. Acta*, 1952, **35**, 520).

2 : 5-Dimethoxybenzyl cyanide was alkylated with di-(2-chlorethyl)methylamine (cf. Eisleb, *Ber.*, 1941, **74**, 1433) to give 4-cyano-4-(2 : 5-dimethoxyphenyl)-1-methylpiperidine which was then reduced to 4-aminomethyl-4-(2 : 5-dimethoxyphenyl)-1-methylpiperidine (I; R = Me). Demethylation with hydrobromic acid gave the dihydroxy-amine (I; R = H). Oxidation with potassium ferricyanide gave a product isolated in high yield which had the composition of the expected indolenine. However, its properties were at variance with this type of structure; in particular it remained unchanged after prolonged

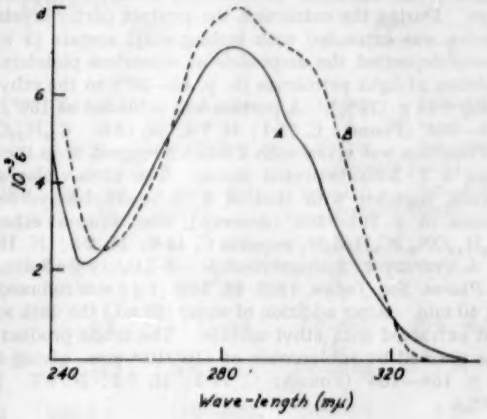


treatment with acid, and the alkaline solution showed little tendency to undergo autoxidation. The ultra-violet absorption spectrum (Figure) was clearly that of an indole and not an indolenine, and was in fact very similar to that of 5-hydroxy-2 : 3-dimethylindole prepared for comparison. Evidently therefore rearrangement had occurred, analogous to the Plancher rearrangement of 3 : 3-disubstituted indolenines in hot acid, and the product was 1 : 2 : 3 : 4 : 5 : 10-hexahydro-7-hydroxy-3-methylazep[4, 5-*b*]indole † (III). The unusual feature in the present case is that the rearrangement occurred in cold neutral solu-

* Parts I and II, *J.*, 1954, 1165, 3651.

† The name and state of hydrogenation accord with Ring Index principles (cf. R.I. no. 1788).

tion. It is suggested that a quinone imine intermediate is first formed (cf. Cromartie and Harley-Mason, *J.*, 1952, 2525); an oxidation–reduction rearrangement of this would lead to an intermediate (II) having an electron-deficient carbon atom at the indole 2-position, giving a favourable situation for rearrangement at the quaternary carbon atom, possibly further facilitated by electron release from the piperidine nitrogen atom. It is noteworthy that a similar situation arises in the intermediate obtained in the synthesis of (±)-eseroline (Part II, *loc. cit.*): in this earlier case, however, rearrangement of the carbon skeleton does not occur since the electron deficiency at the indole 2-position is satisfied by reaction with the second nitrogen atom giving another ring, a possibility which is on steric grounds absent in the presumed intermediate (II).



Ultra-violet absorption spectra of (*A*) 1 : 2 : 3 : 4 : 5 : 10-*hexahydro*-7-*hydroxy*-3-*methylazep*[4, 5-b]*indole* and (*B*) 5-*hydroxy*-2 : 3-*dimethylindole in* 95% *ethanol.*

Experimental

4-*Cyano*-4-(2 : 5-*dimethoxyphenyl*)-1-*methylpiperidine*.—Liquid ammonia (100 ml.) contained in a flask fitted with stirrer, condenser, and dropping funnel was treated with a small crystal of ferric nitrate followed by sodium (0·1 g.). When dissolution was complete, more sodium (2·3 g.) was added in small pieces and the solution stirred until all had dissolved. Dry ether (50 ml.) was then added and the ammonia was allowed to evaporate at room temperature. The ethereal suspension was treated with a solution of 2 : 5-dimethoxybenzyl cyanide (8·0 g.) (Part I, *loc. cit.*) in dry xylene (100 ml.), and the temperature raised slowly to 100°, the ether being distilled off. Heating and stirring were continued for a further 3 hr. until evolution of ammonia had ceased.

Meanwhile a solution of di-(2-chlorethyl)methylamine hydrochloride (9·0 g.) in water (20 ml.) was treated with 2N-sodium hydroxide (22 ml.) with stirring at 0°. The resulting solution was immediately saturated with solid potassium carbonate and extracted with xylene (3 × 50 ml.), and the extracts were dried (K_2CO_3). This solution was added slowly to the deep red suspension prepared as above. The well-stirred mixture was heated at 100° for 5 hr. After cooling, it was extracted with dilute hydrochloric acid (2 × 150 ml.), and the combined extracts were basified with aqueous sodium hydroxide, saturated with potassium carbonate, and extracted with ether (3 × 100 ml.). The ethereal extracts were dried (K_2CO_3), the ether was removed, and the residue distilled, yielding 4-*cyano*-4-(2 : 5-*dimethoxyphenyl*)-1-*methylpiperidine* (5·1 g., 45%) as a colourless highly viscous oil, b. p. 160—165°/0·7 mm. The *hydrochloride* formed prisms, m. p. 233—234° (decomp.; darkening above 220°), from ethanol–ether (Found: C, 60·4; H, 7·3; N, 9·6. $C_{15}H_{20}O_2N_2$,HCl requires C, 60·3; H, 7·1; N, 9·4%).

4-*Aminomethyl*-4-(2 : 5-*dihydroxyphenyl*)-1-*methylpiperidine* (I; R = H).—A solution of the amino-cyanide (4·5 g.) in ethanol (100 ml.) saturated with ammonia at 0° was hydrogenated over Raney nickel at 100°/80 atm. for 5 hr. The catalyst was filtered off, the solvent removed, and the residual oil taken up in ethanol and treated with ethereal hydrogen chloride. The amorphous precipitate formed at first, slowly crystallised, and after two recrystallisations from ethanol–ether yielded 4-*aminomethyl*-4-(2 : 5-*dimethoxyphenyl*)-1-*methylpiperidine dihydrochloride* (3·5 g., 60%) as prisms, m. p. 245—246° (decomp.) (Found: C, 50·2; H, 7·7; N, 8·0. $C_{15}H_{24}O_2N_2$,2HCl,H_2O requires C, 50·6; H, 7·9; N, 7·9%).

The dihydrochloride (3·0 g.) was refluxed with redistilled hydrobromic acid (*d* 1·49; 20 ml.) for 45 min. and the resulting solution diluted with water and evaporated to dryness on the water-bath under reduced pressure of hydrogen. The last traces of water and hydrobromic acid were removed by storage in a vacuum-desiccator over phosphoric oxide and sodium hydroxide, leaving the dihydroxy-diamine dihydrobromide as a light greenish-brown hygroscopic glass which did not crystallise.

1 : 2 : 3 : 4 : 5 : 10-*Hexahydro-7-hydroxy-3-methylazep*[4, 5-*b*]*indole* (III).—To a solution of the dihydroxy-diamine dihydrobromide (0·85 g.) in water (75 ml.), potassium ferricyanide (1·32 g.) and sodium hydrogen carbonate (0·67 g.) in water (75 ml.) were added slowly with stirring. After 10 min. a little sodium dithionite was added and after saturation with salt the light brown solution was extracted continuously with peroxide-free ether (200 ml.) under nitrogen for 2 days. During the extraction the product partly crystallised. After removal of the ether, the residue was extracted with boiling ethyl acetate (3 × 50 ml.), and these extracts on cooling slowly deposited the *azepindole* as colourless platelets. A further quantity was obtained by addition of light petroleum (b. p. 60—80°) to the ethyl acetate mother-liquors, the total yield being 0·34 g. (75%). A portion was sublimed at 150°/10^{-4} mm., giving colourless prisms, m. p. 204—205° (Found: C, 72·1; H, 7·4; N, 13·0. $C_{13}H_{16}ON_2$ requires C, 72·3; H, 7·4; N, 13·2%). No reaction was given with Ehrlich's reagent or in the Hopkins–Cole glyoxylic acid test, indicating a 2 : 3-disubstituted indole. The ultra-violet absorption spectrum is recorded in the Figure, together with that of 2 : 3-dimethyl-5-hydroxyindole. The *dipicrate* formed orange prisms, m. p. 201—203° (decomp.), from aqueous ethanol (Found: C, 44·7; H, 3·8; N, 16·4. $C_{13}H_{16}ON_2,2C_6H_3O_7N_3$ requires C, 44·6; H, 3·3; N, 16·6%).

5-Hydroxy-2 : 3-dimethylindole.—5-Ethoxy-2 : 3-dimethylindole (Keimatsu and Sugasawa, *J. Pharm. Soc. Japan*, 1928, **48**, 348) (1 g.) was refluxed with hydrobromic acid (*d* 1·49; 15 ml.) for 40 min. After addition of water (50 ml.) the dark solution was boiled with charcoal, filtered, and extracted with ethyl acetate. The crude product remaining after removal of the solvent was purified by sublimation at 110°/10^{-4} mm., giving *5-hydroxy-2 : 3-dimethylindole* as needles, m. p. 154—155° (Found: C, 74·3; H, 7·2; N, 9·2. $C_{10}H_{11}ON$ requires C, 74·5; H, 6·8; N, 8·9%).

One of us (A. H. J.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, September 22nd*, 1954.]

The Analytical Properties of 8-Hydroxy-5-, -6-, and -7-trifluoromethylquinoline.

By R. BELCHER, A. SYKES, and J. C. TATLOW.

[Reprint Order No. 5427.]

The sensitivities of 8-hydroxy-5-, -6-, and -7-trifluoromethylquinoline towards selected metal ions have been determined. 8-Hydroxy-5- and -6-trifluoromethylquinoline reacted with the majority of those tested, but the 7-trifluoromethyl isomer did not give a precipitate with any. The relationships between the structures of these hydroxy-compounds and the observed reactions are discussed.

SYNTHESES have been reported for 8-hydroxy-5- (Pettit and Tatlow, *J.*, 1954, 3852), -6-, and -7-trifluoromethylquinoline (Belcher, Stacey, Sykes, and Tatlow, *J.*, 1954, 3846). We now describe and discuss the analytical properties of these compounds.

8-Hydroxyquinoline (" oxine ") has long been used as a reagent in analytical chemistry, but it is not very selective. Many attempts have been made to modify its analytical properties by the introduction of substituent groups into the molecule (see, *e.g.*, Welcher, " Organic Analytical Reagents," D. Van Nostrand Co. Inc., New York, 1947, Vol. 1, p. 323). Only one such derivative, however, 8-hydroxy-2-methylquinoline (Merritt and Walker, *Ind. Eng. Chem. Anal.*, 1944, **16**, 387) exhibits any profound difference from the parent compound: it does not precipitate aluminium. This greater selectivity has been

attributed to its increased molecular size (*idem*, *loc. cit.*). Irving, Butler, and Ring (*J.*, 1949, 1489) studied the analytical properties of 8-hydroxy-2-, -5-, -6-, and -7-methylquinoline, 8-hydroxy-2-phenylquinoline, and some related compounds, and advanced a stereochemical explanation to account for the failure of the 2-methyl derivative to precipitate aluminium. They also noted that 8-hydroxy-7-methylquinoline had an increased sensitivity as compared with oxine and with 8-hydroxy-5- and -6-methylquinoline. Irving and Rossotti (*J.*, 1954, 2910) have, however, shown that the complexes formed by 8-hydroxy-7-methylquinoline are actually less stable than those formed by oxine, again owing, possibly, to steric effects.

TABLE 1.*

Metal used :	Al^{3+}		Cr^{3+}		Fe^{3+}	
Test solution :	A	B	A	B	A	B
Quinoline						
8-OH	4·4—1·7 (*a*)	4·4—1·7	8·4—3·4 (*a*)	16·8—8·4	1·8—0·9 (*a*)	1·8—0·9
8-OH-5-CF_3	97·0—64·5 (lemon-yellow)	64·5—32·0	N.P. (—)	N.P.	3·2—1·6 (greenish-black)	3·2—1·6
8-OH-6-CF_3	0·16—0·06 (lemon-yellow)	0·32—0·16	6·4—3·2 (pale yellow)	12·8—6·4	1·2—0·6 (greenish-black)	1·2—0·6

Metal used :	Cu^{2+}			Zn^{2+}		
Test solution :	A	B	C	A	B	C
Quinoline						
8-OH	1·0—0·4	1·0—0·4 (*a*)	1·0—0·4	1·1—0·4	1·0—0·4 (*a*)	10·6—4·2
8-OH-5-CF_3	1·6—0·65	1·6—0·65 (lime-green)	32·2—16·1	1·6—0·65	1·6—0·65 (white)	N.P.
8-OH-6-CF_3	0·65—0·32	0·65—0·32 (lime-green)	3·2—1·6	1·6—0·65	3·2—1·6 (yellow-green)	N.P.

Metal used :	Ga^{3+}		Mg^{2+}		Ca^{2+}	Th^{4+}	
Test solution :	A	B	B	C	C	A	B
Quinoline							
8-OH	2·3—1·1 (*a*)	2·3—1·1	N.P.	32·0—16·0 (lemon)	64·0—32·0 (yellow)	16·0—6·5	6·5—3·2 (lemon)
8-OH-5-CF_3	6·4—3·2 (pale yellow)	6·4—3·2	64·0—32·0 (white)	N.P.	N.P. (—)	16·0—6·5	6·5—3·2 (lemon-yellow)
8-OH-6-CF_3	3·2—1·6 (pale yellow)	3·2—1·6	32·0—16·0 (lemon)	32·0—16·0	64·0—32·0 (lemon)	1·6—0·65	3·2—1·6 (yellow-green)

Metal used :	WO_4^{2-}	MoO_4^{2-}	VO_3^-		UO_2^{2+}	
Test solution :	A	A	A	B	A	B
Quinoline						
8-OH	64·0—32·0 (white)	6·5—3·2 (white)	64·0—32·0 (green-black)	N.P.	64·0—32·0 (red-brown)	16·0—6·5
8-OH-5-CF_3	128·0—64·0 (white)	64·0—32·0 (yellow)	N.P. (—)	N.P.	6·5—3·2 (red-brown)	6·5—3·2
8-OH-6-CF_3	64·0—32·0 (lemon)	16·0—6·5 (yellow)	32·0—16·0 (green-black)	128·0—64·0	64·0—32·0 (red-brown)	16·0—6·5

For significance of A, B, and C see p. 380.

* N.P. signifies that there was no precipitate of complex. Where a column for test solution A, B, or C is omitted entirely, there was no precipitate with any of the three reagents. Sensitivity limits are given as μg./ml. The colour of the precipitate is given below the sensitivity limits. (*a*) Indicates that these figures are quoted directly from the literature (Irving, Butler, and Ring, *loc. cit.*).

The conditions used for the determination of the sensitivities of the trifluoromethyl-8-hydroxyquinolines followed exactly those of Irving, Butler, and Ring (*loc. cit.*), so a direct comparison could be made with their results. The figures recorded in Table 1 are, for

each combination of reagent and test solution, the smallest concentration (in μg./ml.) of metal ion which gave a precipitate and the largest concentration which just failed to do so under the standardised test conditions. Table 2 lists a further selection of metallic ions which gave precipitates with the reagents.

TABLE 2.

Metal ion used (128·0 μg./ml.)	Colour of precipitate with: 8-hydroxy-5-trifluoromethylquinoline	8-hydroxy-6-trifluoromethylquinoline
Cadmium	White	Pale yellow
Cerium(IV)	Red-brown	Red-brown
Cobalt	White	Yellow
Lead(II)	Pale yellow	Yellow
Manganese	White	Pale yellow
Mercury(II)	Bright yellow	Bright yellow
Nickel	White	Yellow
Silver	Pale yellow	Yellow
Zirconium	Pale yellow	Pale yellow

The sensitivity of 8-hydroxy-6-trifluoromethylquinoline towards the selected metal ions was virtually the same as that of oxine itself. 8-Hydroxy-5-trifluoromethylquinoline, however, was somewhat less sensitive than either of these two compounds. Further, it gave a precipitate with only one metal, copper, in alkaline solution (C), and, even in this case, precipitation was slow and incomplete. Pettit and Tatlow (*loc. cit.*) have, however, shown that 8-hydroxy-5-trifluoromethylquinoline readily loses fluorine, as fluoride ion, in alkaline solution, and during measurements of the dissociation constant (see p. 380) it was found that this hydrolysis occurs in solutions of pH 8 or above. Under the conditions used in the tests, the presence of fluoride ions in the solution was demonstrated, but the expected carboxylic acid could not be isolated. It may be that the trifluoromethyl group was only partially hydrolysed, and that an ether-type polymer was formed by evolution of hydrogen fluoride from the trifluoromethyl and hydroxyl groups of adjacent molecules, or by interaction of trifluoromethyl and phenoxide functions (see Jones, *J. Amer. Chem. Soc.*, 1947, **69**, 2346, for a similar effect with *p*-hydroxybenzotrifluoride). Such a compound would not precipitate metal ions because the hydroxyl function is destroyed, and Berg (*Z. anorg. Chem.*, 1932, **204**, 208) has shown that 8-hydroxyquinoline-5-carboxylic acid will not precipitate metal ions in alkaline solution, so that, in either case, no insoluble metal complexes should be formed.

In contrast with the other isomers, 8-hydroxy-7-trifluoromethylquinoline did not give a precipitate with any of the metals listed in Tables 1 and 2, or with any of the following ions: ammonium, beryllium, bismuth, copper(I), gold(III), iridium, lanthanum, lithium, molybdenum(VI), osmium, palladium, potassium, rhodium, ruthenium, sodium, thallium(I), and tin(II). This failure is rather surprising: extraction of the free hydroxyquinoline from the test solutions in several cases showed that soluble complexes were not formed.

Calvin and Wilson (*J. Amer. Chem. Soc.*, 1945, **67**, 2003), Calvin and Bailes (*ibid.*, 1946, **68**, 949), and Duffield and Calvin (*ibid.*, p. 557) have shown that the basic or acidic strength of an organic compound can have a considerable effect on the stability of its metal complexes. A strong base and a weak acid both have a great tendency to share their electron pairs with metal ions, but the introduction of electron-attracting groups into the molecule will increase the acidic, or decrease the basic, strength, and hence should lower the stability of the complexes. The trifluoromethyl group exerts a strong electron-attracting effect and its introduction into the benzenoid part of an 8-hydroxyquinoline should lead to an increase in the acidity of the phenolic group, and, possibly, to a decrease in the basicity of the heterocyclic nitrogen. The effect on the former should be greatest when the trifluoromethyl group is placed *ortho* or *para*, and least when it is *meta*, to the hydroxyl group. Accordingly, attempts were made to relate the dissociation constants of 8-hydroxyquinoline and the three trifluoromethyl-substituted derivatives to their analytical properties.

Several procedures have been employed for determining the dissociation constants of 8-hydroxyquinolines, the potentiometric titration and the spectrophotometric method

being now the most frequently used (see, *e.g.*, Näsänen, Lumme, and Mukula, *Acta Chem. Scand.*, 1951, **5**, 1199; Irving, Ewart, and Wilson, *J.*, 1949, 2672). Both are equally satisfactory (Vandenbelt, Henrich, and Vandenberg, *Anal. Chem.*, 1954, **26**, 726). Though there have been discrepancies in earlier work, a value of 9·85 ± 0·05 (at 25°) is now accepted for the thermodynamic dissociation constant, pK_A, of the phenolic group of 8-hydroxyquinoline (Näsänen *et al.*, *loc. cit.*; Irving *et al.*, *loc. cit.*). In the present work an orthodox potentiometric titration method was used. In aqueous solution at 25°, the following values for the (Brønsted) acid dissociation constants ($pK_{OH'}$) were obtained: 8-hydroxyquinoline; 9·83 ± 0·11; 8-hydroxy-6-trifluoromethylquinoline, 10·01 ± 0·11; 8-hydroxy-7-trifluoromethylquinoline, 8·99 ± 0·10. Attempts to measure the value of $pK_{OH'}$ for 8-hydroxy-5-trifluoromethylquinoline under these conditions were unsuccessful since the trifluoromethyl group is extremely sensitive to alkali (Pettit and Tatlow, *loc. cit.*). In solutions of pH 8 or above, fluoride ion was liberated and the solution became brown. The dissociation constants of the trifluoromethyloxines were measured also in 50% aqueous ethanol, since under these conditions the attack on the trifluoromethyl group of the 5-isomer was somewhat less rapid at pH 8—9, and an approximate value for the constant could then be obtained. The relative acidities of the other compounds were in the same order as in aqueous solution, and the 5-isomer consistently gave the lowest value for $pK_{OH'}$, though the reproducibility of the results was not good, showing that some decomposition was probably proceeding. Thus, 8-hydroxy-6-trifluoromethylquinoline is very similar to oxine in its acid strength, but the other two isomers are more acidic; it is probable that the 5-trifluoromethyl isomer is the strongest acid of the three. Irving and Rossotti (*loc. cit.*) have shown that $pK_{OH'}$ values in aqueous dioxan for 8-hydroxy-5-, -6-, and -7-methylquinoline and for oxine are, respectively, 11·11, 10·71, 11·31, and 10·80. Here the inductive effects are, of course, opposite to those in the fluoro-derivatives, and it is of interest that the 6-isomers in each case appear to be very slightly anomalous. The dissociation constants of the $:NH^+$ groups of the 8-hydroxyquinolinium ions were also measured in aqueous solution at 25° and were: 5·0 ± 0·1 for 8-hydroxyquinoline, and 1·8 ± 0·2, 2·6 ± 0·3, and 2·4 ± 0·4 for the 5-, 6-, and 7-trifluoromethyl derivatives, respectively. The potentiometric method is probably less suitable for measurement of basic dissociation constants of this type than for acidic ones (cf. Vandenbelt *et al.*, *loc. cit.*) and no great accuracy is claimed for the values given above. However, it appears reasonably certain that the trifluoromethyl group has a surprisingly large effect on the basicities of the heterocyclic nitrogen functions. This would be in accord with the effect, on the acidities of certain benziminazoles, of trifluoromethyl groups carried on the benzenoid ring (Belcher, Sykes, and Tatlow, *J.*, 1954, 4159).

Thus the acidic dissociation constants of 8-hydroxy-5- and -6-trifluoromethylquinoline and of oxine itself are in general accord with the relative abilities of the compounds to give insoluble complexes. It seems, however, that the weakly basic characters of these two trifluoromethyl-oxines cannot have a great effect on their properties as precipitants. The 7-trifluoromethyl isomer is clearly abnormal in its analytical properties, and it is very unlikely that its comparatively low acidity is the reason for this. Also, though it is a weak base, its basicity is comparable with those of its isomers, so that this also does not appear to explain its behaviour. Another apparent abnormality of the compound lies in its m. p., which is some 150° higher than those of the isomers, though in similar *O*-derivatives of the three phenols the m. p.s are of the same general order. The abnormalities probably arise from *ortho*-effects such as steric factors, or intramolecular hydrogen bonding between the hydroxyl and trifluoromethyl groups. Jones (*loc. cit.*) postulated an effect similar to the latter to account for the unusually low b. p.s of *o*-hydroxy- and *o*-amino-benzotrifluoride. The trifluoromethyl group is larger than the methyl group, from which it has been postulated that steric effects may arise (Irving and Rossotti, *loc. cit.*) and this size might be sufficient to prevent the formation of insoluble complexes. However, other 7-substituted oxines with relatively large substituents, in particular bromo- and iodo-derivatives, do, in some cases, give precipitates with metal ions (Yoe and Sarver, "Organic Analytical Reagents," John Wiley and Sons, New York, 1941, p. 238; Welcher, *op. cit.*; Albert and Magrath, *Biochem. J.*, 1947, **41**, 534).

Experimental

Preparation of Reagents.—8-Hydroxy-5-, -6-, and -7-trifluoromethylquinoline were prepared as described by Pettit and Tatlow (*loc. cit.*) and Belcher, Stacey, Sykes, and Tatlow (*loc. cit.*).

Testing of Reagents.—(a) *Composition of test solutions.* Solutions A, B, and C were prepared as described by Irving, Butler, and Ring (*loc. cit.*). The solutions of metal ions were prepared from "AnalaR" and "Specpure" compounds. Each organic reagent was used as a 0·1M-solution in ethyl alcohol.

(b) *Procedure.* Portions (1·0, 0·5, 0·25, and 0·1 ml.) of metal solution (0·4 mg./ml.) were placed in four test-tubes together with solution A (2·0 ml.), ethyl alcohol (1·0 ml.), the reagent solution (0·2 ml.), and sufficient water to give a final volume of 6·2 ml. A fifth tube contained reagent, ethyl alcohol, and water so that the behaviour of the reagent alone could be observed, whilst a sixth tube contained metal solution, ethyl alcohol, and water, to indicate the behaviour of the metal ions alone. Each tube was heated at 80° for 15 min., and then cooled before being examined for precipitation. When a precipitate was formed in the solution containing 0·1 ml. of 0·4 mg./ml. metal-ion solution, the tests were repeated with more dilute metal-ion solutions (0·04 mg./ml., and then 0·004 mg./ml.). This sequence of testing was then repeated for each metal in each solution, and for each reagent. The sensitivities recorded by Irving, Butler, and Ring (*loc. cit.*) were unaffected by the replacement, in the test solution, of water (1·0 ml.) by ethyl alcohol (1·0 ml.). These results are given in Table 1.

Test solutions containing the 7-trifluoromethyl isomer and certain of the metal ions were extracted with chloroform, and in each case the quinolinol was recovered in good yield. The metals examined in this way were calcium (solutions A, B, and C), copper(II) (A, B, and C), iron(III) (A, B, and C), uranyl (B and C), and zinc (A and C).

Other Metals tested.—The metals listed in Table 2 were shown to give precipitates in solution A by the following procedure: The metal-ion solution (2·0 ml.), solution A (2·0 ml.), ethyl alcohol (1·0 ml.), water (1·0 ml.), and reagent solution (0·2 ml.) were placed in a test-tube and heated at 80° for 15 min. The tube was cooled and the formation and colour of the precipitate were observed. The procedure was repeated for each metal and each reagent.

This procedure was also applied to the tests carried out on 8-hydroxy-7-trifluoromethylquinoline, with these and other metals, in solutions A, B, and C.

Measurements of Dissociation Constants.—In the determinations of pK_{OH}', in aqueous solution, the compounds (about 0·1 g.) in approx. 0·05N-sodium hydroxide (20 c.c.) were titrated against approx. 0·1N-hydrochloric acid at 25° ± 0·1°. A blank determination, identical except that the compound was omitted, was done in each case. The pH was measured by using a glass electrode (Doran Type M 4999) and a saturated calomel electrode, with a saturated potassium chloride bridge, in conjunction with a pH meter [Marconi Type TF 717A, standardised against 0·05M-potassium hydrogen phthalate (pH 4·005) and 0·05M-sodium borate (pH 9·18)]. The titrations were done in a sealed Polythene vessel, and nitrogen was bubbled through the solutions. The dissociation constants were calculated from the volumes of alkali bound, *i.e.*, the differences between the sample titration and the blank titration, at various pH values near the half-neutralisation point. Each compound was tested in several independent runs, and the constants quoted are average ones with the limits defining the highest and lowest values obtained. No reliable figures for pK_{OH}' could be measured for the 5-trifluoromethyl isomer, since fluoride ion was liberated and a brown colour formed in solutions of pH greater than 8. The effect occurred also when alkali was added to a solution of the compound in acid.

Values for the acid dissociation constants were obtained also in 50% aqueous ethyl-alcoholic solutions by direct titration with alkali (approx. 0·1N). Basic dissociation constants were measured by titration of the compound (about 0·1 g.) in 0·05N-hydrochloric acid, with 0·1N-sodium hydroxide. In both of these series of measurements the "solvent correction" was applied.

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The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part VI. Derivatives of* 1 : 2 : 3 : 4-*Tetrahydro-1-methyl-4-oxoquinoline.*

By JOHN T. BRAUNHOLTZ and FREDERICK G. MANN.

[Reprint Order No. 5670.]

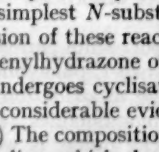
The phenylhydrazone of the above ketone, when subjected to the Fischer indolisation, gives a ψ-indoloquinoline: the diphenylhydrazone gives a true indoloquinoline, in which the ·NMe·CH_2· group is readily oxidised to the ·NMe·CO· group, a novel type of oxidation in this series.

The parent ketone, when subjected to the Pfitzinger reaction with alkaline isatin, gives the scarlet quinolinoquinolinecarboxylic acid (IX) which on decarboxylation gives the yellow base (X). Conditions necessary for the "allylic rearrangement" of both compounds have been determined, and the isomeric acids, bases, and monohydrochlorides of each have thus been isolated. This type of isomerism has not previously been detected in such simple compounds.

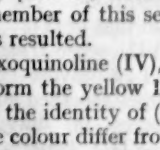
Both isomeric bases undergo an oxidation similar to that noted above, with the formation of the same product (XVI).

In view of these results, the structure of certain analogous compounds has been briefly reinvestigated.

In Part I (Mann, *J.*, 1949, 2816) it was shown that 1 : 2 : 3 : 4-tetrahydro-4-oxo-1-phenylquinoline (as IV) gave a phenylhydrazone which on Fischer cyclisation gave a yellow ψ-indole, which underwent aromatisation with acids to give colourless salts; further, the oxo-quinoline reacted with isatin in alkaline solution to give a carboxylic acid (as IX), which by decarboxylation gave an amine (as X) in which the ·NPh·CH_2· group underwent very ready oxidation to the –NPh·CO– group. In Part II (Mann and Smith, *J.*, 1951, 1898), a novel feature in these reactions appeared: it was shown that 1-oxojulolidine, similarly treated with alkaline isatin, gave an acid undergoing decarboxylation to quinolino-(2′ : 3′-1 : 2)juloline (I), which, however, when heated with acids gave the isomeric base (II), reconverted by heat into (I). Both isomers readily gave the same oxidation product (III).



(I)



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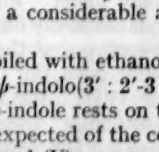


(III)

We have now investigated in some detail the comparable reactions of 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline (IV) (Allison, Braunholtz, and Mann, *J.*, 1954, 403), as being the simplest *N*-substituted member of this series, and a considerable amplification and extension of these reactions has resulted.

The phenylhydrazone of the 4-oxoquinoline (IV), when boiled with ethanolic hydrogen chloride, undergoes cyclisation to form the yellow 1-methyl-ψ-indolo(3′ : 2′-3 : 4)quinoline (V). The considerable evidence for the identity of (V) as a ψ-indole rests on the following points. (i) The composition and the colour differ from those expected of the corresponding indoloquinoline, which should be colourless. (ii) The compound (V) very readily forms a stable colourless monohydrochloride having, it is suggested, the structure (VI; X = Cl); by this process the molecule undergoes aromatisation, and the structure (VI) would undoubtedly require loss of colour. The compound (V) also readily forms a colourless methiodide and ethiodide, similar to (VI; X = I) but with the ·NH· group replaced by ·NMe· and ·NEt· respectively. (iii) The compound (V), when crystallised from aqueous

* Part V, *J.*, 1952, 1870.

ethanol, forms a pale yellow hydrate, whose colour deepens on dehydration, although sublimation at 0·1 mm. is necessary to obtain the anhydrous (V): this colour change is rapidly reversed by shaking a suspension of (V) in water, or more slowly by exposing the powdered (V) to the atmosphere. It is highly probable that the ψ-compound (V), which is clearly an "anhydronium base" (cf. Robinson and Thornley, *J.*, 1924, **125**, 2169; Armit and Robinson, *J.*, 1925, **127**, 1604; Robinson, *J.*, 1929, 2947), exists in the hydrated form largely as (VI; X = OH). Strong evidence for this is obtained from the absorption spectra of (V) in anhydrous light petroleum, in 95% ethanol, and in 0·1N-hydrochloric acid [Fig. 1, in which the intensities in petroleum have been arbitrarily selected, because of the very low solubility of (V) in this solvent]. The spectrum of (V) in petroleum is markedly different from that in the acid, to which, however, the spectrum in ethanol shows considerable resemblance. (iv) The infra-red spectrum of the ψ-indole (V) shows no bands below 6 μ, and hence the ·NH· group must be absent; between 6 and 10 μ the spectrum is rather complex, but there are strong bands at 6·10 and 6·25 μ [cf. (XV), p. 384]: the hydrochloride (VI; X = Cl) was too hygroscopic to allow the presence of the ·NH· band to be

FIG. 1. FIG. 2.

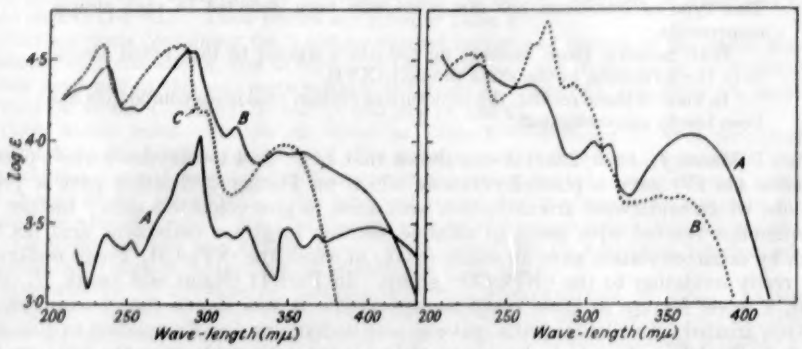


FIG. 1. 1-*Methyl-ψ-indolo*(3′ : 2′-3 : 4)*quinoline* (V) *in* (*A*) *light petroleum* (ε *values arbitrary*), (*B*) *in* 95% *ethanol*, (*C*) *in* 0·1N-HCl.

FIG. 2. *A*, 1 : 2-*Dihydro*-1-*methyl*-1′-*phenylindolo*(3′ : 2′-3 : 4)*quinoline* (VII) *in* 95% *ethanol*. *B*, 1 : 2-*Dihydro*-1-*methyl*-2-*oxoquinolino*(3′ : 2′-3 : 4)*quinoline* (XVI) *in* 95% *ethanol*.

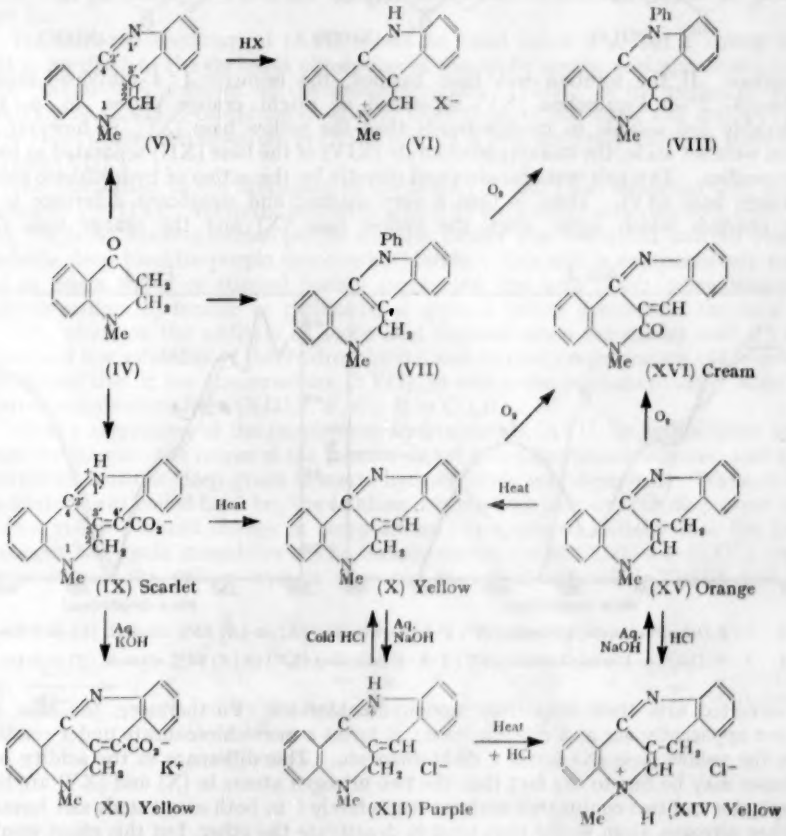
decisively determined. (v) Kermack and Storey's entirely different synthesis (*J.*, 1950, 607) of the ψ-indole (V) affords strong support for the above structure.

The conversion of the phenylhydrazone of (IV) into the ψ-indole (V) involves a dehydrogenation, which could not occur if, for example, the diphenylhydrazone were used. We find that the latter gives 1 : 2-dihydro-1-methyl-1′-phenylindolo(3′ : 2′-3 : 4)quinoline (VII), which, as expected, is colourless, does not form a stable hydrochloride, and forms a methiodide only under "forcing" conditions. The ultra-violet absorption spectrum of (VII) (Fig. 2) is markedly different from that of (V).

It is noteworthy that the indole (VII), when treated with potassium permanganate in acetone, readily gave the colourless 1 : 2-dihydro-1-methyl-2-oxo-1′-phenylindolo(3′ : 2′-3 : 4)quinoline (VIII), the first example recorded of this type of oxidation in indoloquinolines, although several examples in dihydroquinolinoquinolines are known (cf. Parts I—V). The oxoquinoline (VIII), being a cyclic acid amide, is weakly basic and did not give a 2 : 4-dinitrophenylhydrazone; its infra-red spectrum showed a strong band at 6·06 μ, due to the amide CO group [cf. (XVI) below].

When the oxoquinoline (IV) was condensed with isatin in hot alkaline solution, acidification then gave 1 : 2-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid (IX) as deep scarlet very slightly soluble crystals, which underwent decarboxylation by heat to form the vividly yellow crystalline 1 : 2-dihydro-1-methylquinolino(3′ : 2′-3 : 4)-quinoline (X), m. p. 98—100°.

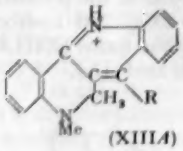
It is significant that the scarlet acid (IX) gave a yellow potassium salt (XI), whereas the yellow base (X) gave a stable purplish-red monohydrochloride (XII). There is no doubt therefore that the acid (IX) exists as a zwitterion, receiving contributions from the forms (XIII*A*, *B*, *C*; R = CO_2^-): this zwitterion formation is destroyed in the potassium salt (XI), the colour of which therefore resembles that of the base (X). The hydrochloride (XII) of this base has a cation receiving similar contributions by the forms (XIII*A*, *B*, *C*; R = H) and hence has a colour resembling that of the zwitterion acid (IX).



Further confirmation of these structural changes is provided by an acetone solution of the base (X), which when treated with hydrogen chloride rapidly acquired a deep red colour which faded as the passage of chloride continued, and ultimately the colourless solution deposited fine colourless needles, undoubtedly of the dihydrochloride of (X), in which the above resonance could not occur; this salt was so unstable that it reverted to the red monohydrochloride (XII) immediately on removal from the acid solution. Similarly the base dissolved in concentrated hydrochloric acid to a colourless solution, which on dilution with water, ethanol, or acetone immediately became deep reddish-purple. By the use of concentrated solutions of chloroplatinic and chloroauric acid, however, unstable salts corresponding to the dihydrochloride have been isolated.

The acid (IX) and the base (X) both show an isomerism comparable with that of quinolino(2′ : 3′-1 : 2)juloline (I), and which has not hitherto been detected in these simpler compounds. The isomerism of the base (X) will be discussed first.

When a solution of the yellow base (X) in an excess of dilute hydrochloric acid, or an aqueous solution of the purple monohydrochloride (XII), was boiled under nitrogen, the purple colour rapidly changed to reddish-orange and finally to yellow, with a greenish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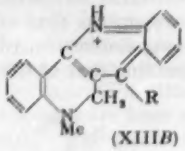
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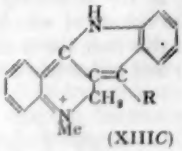
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fluorescence. If the solution was then basified, the isomeric 1 : 4′-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline (XV) separated as bright orange plates, m. p. 155°, considerably less soluble in most solvents than the yellow base (X): if, however, the solution were set aside, the monohydrochloride (XIV) of the base (XII) separated as bright yellow needles. This salt was also obtained directly by the action of hydrochloric acid on the orange base (XV). There is thus a very marked and significant difference in the colour changes which occur when the yellow base (X) and the orange base (XV)

FIG. 3.

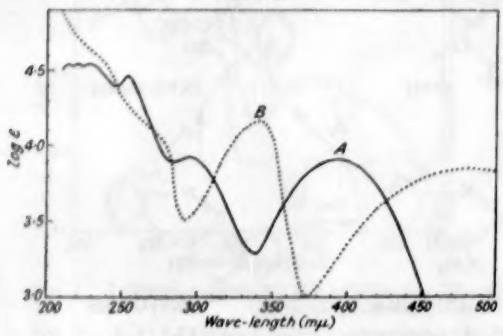


FIG. 4.

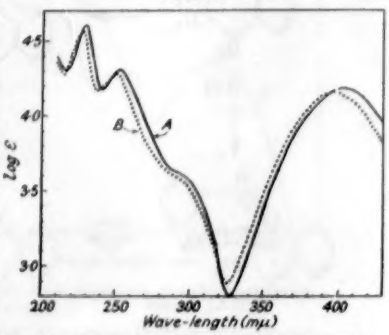


FIG. 3. 1 : 2-*Dihydro*-1-*methylquinolino*(3′ : 2′-3 : 4)*quinoline* (X) *in* (*A*) 95% *ethanol*, (*B*) *in* 0·1N-HCl.

FIG. 4. 1 : 4′-*Dihydro*-1-*methylquinolino*(3′ : 2′-3 : 4)*quinoline* (XV) *in* (*A*) 95% *ethanol*, (*B*) *in* 0·1N-HCl.

are converted into their respective monohydrochlorides. Furthermore, the base (XV) does not apparently act as a diacidic base: it forms a monochloroaurate under conditions where the yellow base (X) forms a dichloroaurate. This difference in the acidity of the two bases may be due to the fact that the two nitrogen atoms in (X) and (XV) are linked through one and two conjugated systems respectively: in both compounds salt formation on either nitrogen atom would thus tend to deactivate the other, but this effect would be stronger in (XV) than in (X). Finally, the orange base (XV) when heated in a vacuum distilled with conversion into the yellow base (X), the greater thermal stability of which is probably due to its higher degree of aromatic character [cf. (I) and (II)].

Neither the infra-red spectrum of (X) nor that of (XV) shows any significant band below 6 μ, and the ·NH· group is therefore absent in both. Whereas that of (X) shows a moderately strong band at 6·23 μ with weaker bands at 6·16 and 6·34 μ, that of (XV) shows a strong and very sharp band at 6·1 μ, which also appears in that of the ψ-indole (V): it is probable that this band is due to the conjugated ·N:C·C:C·N· system present in both compounds.

The ultra-violet spectra (Fig. 3) of the base (X) and of its hydrochloride (XII) differ of course very considerably, indicating a marked difference in their fundamental structures. By contrast, the spectra (Fig. 4) of the base (XV) and its hydrochloride (XIV) are almost identical, indicating that salt formation has occurred without structural change: conse-

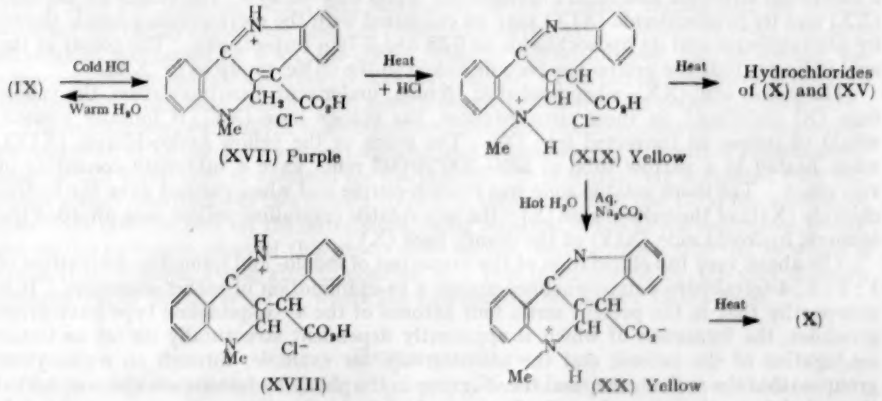
quently the cation must have been formed by proton addition to the ·NMe· group and not to the 1'-N atom, since the latter addition would allow resonance comparable in character with (XIII*A*, *B*, and *C*) and thus give a deeply coloured salt.

Oxidation of the base (X) or the base (XV) in acetone with potassium permanganate or in benzene with air readily yielded the cream-coloured 1 : 2-dihydro-1-methyl-2-oxoquinolino(3' : 2'-3 : 4)quinoline (XVI): however, the base (X) in acetone containing a large excess of hydrogen peroxide underwent no oxidation during 1 week, a result unaffected by making the solution weakly basic or acidic (a similar result is recorded in Part I).

The infra-red spectrum of (XVI) shows no band below 6 μ, but a strong band at 6·04 μ, ascribed to the carbonyl absorption of the cyclic amide, and apparently identical with that at 6·06 μ shown by the indole derivative (VIII); in the region 6—10 μ the spectrum of (XVI) is considerably simpler than those of the bases (X) and (XV). The ultra-violet absorption spectrum of (XVI) (Fig. 2) is also markedly different from those of (X) and (XII).

The elucidation of the isomerism of the bases (X) and (XV) simplifies that shown by the scarlet acid (IX). When the powdered acid (IX) was ground with cold 20% hydrochloric acid, the latter became intense purple and the former was converted into an even more insoluble deep blackish-purple monohydrochloride. This salt is comparatively unstable, and in warm water or ethanol readily regenerates the acid (IX); when treated with aqueous sodium hydroxide or carbonate, it gives a yellow solution of the sodium salt (as XI), which on the addition of acetic acid deposits again the scarlet acid (IX). The colour and low solubility of this hydrochloride, and its ready regeneration of the acid (IX), all indicate that it has the structure (XVII), in which the resonance cation would again receive contributions from (XIII*A*, *B*, *C*; R = CO_2H).

When a suspension of the purple monohydrochloride (XVII) in hydrochloric acid was boiled for 30 min., the colour of the solution faded to a pale yellowish-brown, and a highly crystalline insoluble deep green isomeric hydrochloride was deposited. When, however, the mixture was boiled for 7 hr., the solution became very pale and the deep green crystals became yellow without change in composition. It appeared initially that the hot acid treatment had again caused the allylic transformation [as in (XII) ⟶ (XIV)], and that the green and the yellow crystals were the monohydrochlorides (XVIII) and (XIX)



respectively. The following evidence indicates strongly, however, that the green and the yellow crystals represent solely dimorphic forms of the monohydrochloride (XIX). (i) The yellow crystals have m. p. 250°. The green crystals, when heated, become progressively more yellow between 160° and 200° and ultimately melt at 250°; when immersed even at 240°, the colour change occurs before melting. A mixture of the two forms has m. p. 250°. (ii) The green crystals, heated at 200°/0·01 mm., are transformed completely into

the yellow crystals. (iii) The green crystals when finely crushed give a greenish-yellow powder. (iv) The two forms, suspended as a mull in paraffin, give identical infra-red spectra. (v) In no circumstances did the green or the yellow hydrochloride regenerate the scarlet acid (IX): both dissolved in aqueous sodium hydroxide to give a bright yellow solution, which underwent no appreciable change on treatment with acetic acid [cf. the behaviour of (XVI)]. (vi) A solution of either form in warm dilute sodium carbonate, or in hot water, on cooling, deposited the bright yellow crystalline 1 : 4′-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid (XX): this acid was also obtained when solutions of the hydrochlorides in aqueous sodium hydroxide were treated with an excess of carbon dioxide.

The above evidence shows almost conclusively that the colour of the green crystals is due solely to surface reflexion and thus has no fundamental constitutional significance. The insolubility (without chemical change) in all liquids prevents observation of the true colour by transmitted light: the properties of the salt are, however, in marked contrast to those of the scarlet acid (IV), which when finely crushed still retains its deep red colour, and, although also insoluble in almost all liquids, gives in boiling acetic acid a very dilute saturated solution which is still deeply red. Examples of compounds existing in two crystalline forms of different colour are not rare. Huang-Hsinmin and Mann (*J.*, 1949, 2908) have recorded two cyanine dyes, each of which exists in two crystalline forms which are markedly different in colour but have the same m. p. and give identical solutions in cold solvents; in one case the particular crystalline form obtained depended solely on the solvent employed for crystallisation.

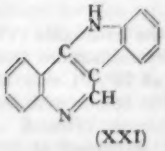
The constitution (XIX) is allocated to the yellow monohydrochloride, for the alternative structure (XVIII) would possess marked resonance and cause the salt to show intense colour in the solid state and in solution. There is strong evidence that the yellow acid (XX) has the zwitterion structure indicated. The infra-red spectrum of the yellow monohydrochloride (XIX) shows a strong band at 5·85 μ, which must be attributed to the carbonyl function of the non-ionised carboxyl group; in phenylacetic acid, of which (XIX) may be regarded as a derivative, the corresponding band occurs at 5·87 μ. The infra-red spectrum of the acid (XX), shows broad absorption centred at 3·05 μ, due to $\equiv NH^+$, and has two bands at 6·11 and 6·24 μ; the latter, which is appreciably the stronger, is attributed to the carboxylate ion of the zwitterion (XX). This band is characteristic of amino-acids having a zwitterion structure and occurs between the limits 6·21—6·38 μ; the values for the acid (XX) and its hydrochloride (XIX) may be compared with the corresponding bands shown by phenylglycine and its hydrochloride at 6·38 and 5·78 μ respectively. The colour of the acid indicates that the proton has become linked to the ·NMe· group as in (XX).

The yellow acid (XX), when heated at 15 mm., underwent decarboxylation, the yellow base (X) distilling: in these circumstances, the orange base (XV), if initially formed, would of course be converted into (X). The green or the yellow hydrochloride (XIX), when heated in a narrow tube at 250—300°/0·003 mm., gave a sublimate consisting of two zones. The more volatile zone was reddish-purple and when purified gave the hydrochloride (XII) of the yellow base (X); the less volatile crystalline yellow zone afforded the isomeric hydrochloride (XIV) of the orange base (XV).

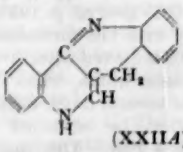
The above very full elucidation of the isomerism of indolo- and quinolino-derivatives of 1 : 2 : 3 : 4-tetrahydro-4-oxoquinolines invites a re-examination of earlier examples. It is noteworthy that in the present series four ketones of the 4-oxoquinoline type have given ψ-indoles, the formation of which is apparently dependent structurally on (*a*) an initial conjugation of the ketonic and the amino-group, for example, through an *o*-phenylene group, so that the amino-group and the ·N: group in the phenylhydrazone are also conjugated [1-methyl-4-oxopiperidine phenylhydrazone, which lacks this factor, gives a normal indole (Cook and Read, *J.*, 1945, 399)], and (*b*) an orientation of the two fused heterocyclic rings in the indolo-system such that dehydrogenation will further conjugate the two nitrogen atoms [as in (V)].

The compound obtained by Clemo and Perkin (*J.*, 1924, **125**, 1608) from 1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline is structurally unique, however, since the ketone has the unsubstituted ·NH· group. Although on indolisation two hydrogen atoms were lost, the

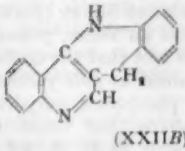
properties of the indolo-derivative (colourless crystals) show that the mobile hydrogen has now allowed aromatisation by giving the structure (XXI) and that, as expected, a ψ-indole has not been formed.



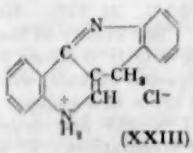
(XXI)



(XXII*A*)



(XXII*B*)



(XXIII)

The properties of the red 1 : 2-dihydroquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid which Clemo and Perkin (*loc. cit.*) obtained by the action of alkaline isatin on their ketone show that its constitution is as (IX). We find, however, that when the purple-red solution of this acid in hydrochloric acid is boiled, the colour rapidly fades and the precipitated yellow material, when suitably crystallised, affords the isomeric 1 : 4-dihydroquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid (as XX); the same isomerisation is readily induced by heating the red acid at 170—175°/15 mm., and therefore always occurs before the acid melts.

On the other hand, the yellow base obtained by Clemo and Perkin by decarboxylation of their red acid, dissolves in hot hydrochloric acid to a yellow solution, which deposits a bright yellow crystalline monohydrochloride, from which the yellow base can readily be regenerated. These properties indicate strongly that the allylic transformation has already occurred in this base. This is confirmed by the fact that the ultra-violet spectra of this base and our orange base (XV) in ethanol show some resemblance, but in 0·1N-hydrochloric acid are almost identical. Although Clemo and Perkin's base may thus have structure (XXII*A* or *B*), the former is more probable, the monohydrochloride then having the structure (XXIII).

Although the isomerisation of the acid and the base is thus far more rapid in the ·NH· series than in the ·NMe· series, a brief reinvestigation of the ·NPh· series (Mann, *loc. cit.*) indicates great stability. The red 1-phenyl acid (as IX) in ethanolic hydrochloric acid gave a solution which was reddish-purple, with a purplish fluorescence, and was unaffected by 4 hours' boiling under reflux. The yellow 1-phenyl base (as X) in hydrochloric acid gave a deep red solution, which was unaffected by 15 minutes' boiling and on cooling deposited the highly crystalline deep red hydrochloride (as XII). When, however, the deep red solution was boiled for 6 hr., the colour faded to yellowish-brown and, on cooling, the isomeric yellow monohydrochloride (as XIV) crystallised. This salt on treatment with alkali liberated an orange base, which again gave a bright yellow solution in hydrochloric acid.

The mechanism of the allylic rearrangement in the above compounds remains uncertain. Consideration of all the known cases indicates that a hetero-atom in position 1, sufficiently basic for salt formation, is essential for the change. It is tentatively suggested that this change occurs essentially in two steps: (i) proton migration from the 1′- to the 1-nitrogen atom: the positive pole on the latter atom, being adjacent to the allylic methylene group, renders the hydrogen atom of this group more mobile, and catalyses step (ii), in which a proton from position 2 migrates to position 4′. This is supported by the very sluggish isomerisation in the ·NPh· series, where the 1-nitrogen atom is very feebly basic.

Experimental

Certain compounds gave consistent m. p.s only in evacuated sealed tubes, noted as (E.T.); in certain cases the tubes had to be immersed in a preheated bath, and the immersion temperature is noted as (I.T. $x°$). Molecular weights were determined ebullioscopically in acetone.

1-*Methyl-ψ-indolo*(3′ : 2′-3 : 4)*quinoline* (V).—Ethanol, saturated with hydrogen chloride (35 c.c.), was added to a mixture of 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline phenylhydrazone (3·2 g.) and ethanol (15 c.c.), which was then boiled under reflux for 5·5 hr., the initial deep orange colour fading considerably. The solution was set aside at 5° overnight, and the

colourless precipitate collected. This was dissolved in water and the solution was basified. The precipitated yellow *ψ*-indole (V) was recrystallised from aqueous ethanol and finally purified by sublimation at 210—230°/0·1 mm., and obtained as lemon-yellow crystals, m. p. 193·5—194° (Found: C, 82·9; H, 4·9; N, 12·1%; *M*, 228. Calc. for $C_{16}H_{12}N_2$: C, 82·7; H, 5·2; N, 12·1%; *M*, 232). Kermack and Storey (*J.*, 1950, 607) give m. p. 195°.

The avidity of the indole for water, presumably with the formation of the hydroxide (VI; X = OH), is shown by the fact that the crude material, even after five recrystallisations from aqueous ethanol, was obtained as pale yellow crystals, which, when dried at 70°/0·1 mm. for 5 hr. or in a vacuum over phosphoric anhydride for several days, darkened in colour with loss of weight and crystal shape, but could not thus be obtained anhydrous (Found, in 3 preparations: C, 81·6, 82·0, 81·5; H, 5·2, 5·35, 4·9%). This material, immersed at 50°, melted at 105—125°, resolidified at 125—150°, and remelted at 195°; immersed at 150°, it immediately melted with effervescence and without resolidification. The sublimed material, exposed to the air for 10 days, became pale and, immersed at 155°, melted with effervescence, resolidified, and remelted at 190—192°.

The colourless precipitate in the above preparation, when recrystallised from ethanol containing 10% of water, afforded colourless hygroscopic needles, m. p. 297° (I.T. 285°), of the *hydrochloride hemihydrate* (VI; X = Cl) (Found: C, 68·8; H, 5·3; N, 10·0. $C_{16}H_{12}N_2$,HCl,0·5H_2O requires C, 69·2; H, 5·1; N, 10·1%).

The indole gave a *picrate*, yellow needles, m. p. 325° (decomp.), from aqueous dimethylformamide (Found: C, 57·4; H, 3·4; N, 15·0. $C_{16}H_{12}N_2$,$C_6H_3O_7N_3$ requires C, 57·3; H, 3·3; N, 15·2%); it also gave a colourless crystalline sulphate which could not be purified.

A methanolic solution of (V), when boiled with methyl iodide under reflux for 30 min., deposited a cream-coloured solid which, twice recrystallised from methanol, gave 1-*methyl*-*ψ*-*indolo*(3′ : 2′-3 : 4)*quinoline methiodide*, colourless needles, m. p. 315—320° (E.T., I.T. 307°) (Found: C, 54·4; H, 4·3; N, 7·6. $C_{17}H_{15}N_2I$ requires C, 54·55; H, 4·05; N, 7·5%). The *ethiodide*, similarly prepared with 3 hours' boiling and recrystallised from methanol, formed a methanol *solvate*, colourless plates, m. p. 298° (effervescence, E.T.) (Found: C, 54·1; H, 3·8; N, 6·7. $C_{18}H_{17}N_2I$,CH_4O requires C, 54·2; H, 5·0; N, 6·65%); when recrystallised from aqueous ethanol and rigorously dried, it formed an ethanol *solvate* of identical m. p. (Found: C, 55·1; H, 4·7. $C_{18}H_{17}N_2I$,0·5C_2H_6O requires C, 55·4; H, 4·9%). This salt gave the *ethopicrate*, intensely yellow crystals, m. p. 200—260° (E.T., I.T. 155), from aqueous ethanol (Found: C, 58·6; H, 3·8; N, 14·0. $C_{24}H_{19}O_7N_5$ requires C, 58·9; H, 3·9; N, 14·3%).

1 : 2-*Dihydro*-1-*methyl*-1′-*phenylindolo*(3′ : 2′-3 : 4)*quinoline* (VII).—A solution of the crude ketone (3 g.) and *as.*-diphenylhydrazine (5·6 g.) in ethanol (25 c.c.) containing acetic acid (0·3 c.c.) was boiled under reflux for 6 hr. and then diluted with water (*ca.* 5 c.c.). Cooling and vigorous stirring gave the *diphenylhydrazone* (4·5 g.) which after crystallisation from ethanol formed bright yellow crystals, m. p. 112—113° (Found: C, 80·8; H, 6·2; N, 13·1. $C_{22}H_{21}N_3$ requires C, 80·7; H, 6·45; N, 12·85%).

This diphenylhydrazone, when indolised as described above, gave a reaction mixture which was filtered whilst hot and diluted with water; the precipitated solid, when recrystallised from ethanol, afforded 1 : 2-*dihydro*-1-*methyl*-1′-*phenylindolo*(3′ : 2′-3 : 4)*quinoline* (VII), cream-coloured plates, m. p. 152—153° (E.T.) (Found: C, 84·8; H, 5·8; N, 9·0%; *M*, 302. $C_{22}H_{18}N_2$ requires C, 85·15; H, 5·85; N, 9·0%; *M*, 310). The indole, when slowly heated in an open tube, had m. p. 210—215°, showing that almost complete atmospheric oxidation to (VIII) (see below) had occurred. Ethanolic solutions of the pure indole had a marked blue fluorescence.

All attempts to isolate a hydrochloride of (VII) failed. The indole gave a *picrate*, bright orange needles (from methanol), m. p. 208·5—209° (Found: C, 62·6; H, 4·0; N, 12·85. $C_{22}H_{18}N_2$,$C_6H_3O_7N_3$ requires C, 62·35; H, 3·9; N, 13·0%); exposure to the air caused the colour to become dull yellowish-brown. When a solution of the indole in an excess of methyl iodide was boiled under reflux for 2 hr., the indole was recovered unchanged. When this solution was diluted with nitromethane and similarly boiled under nitrogen, evaporation gave a solid deposit, which, recrystallised from aqueous methanol, afforded the *methiodide*, colourless needles, m. p. 141° (effervescence) (Found: C, 60·9; H, 4·4; N, 5·95. $C_{23}H_{21}N_2I$ requires C, 61·1; H, 4·7; N, 6·2%).

Oxidation. A solution of the indole (VII) (0·3 g.) in acetone (25 c.c.) was boiled under reflux for 3 hr. during which potassium permanganate in acetone was periodically added to maintain a slight excess. The solution, when filtered, concentrated, and cooled, deposited 1 : 2-*dihydro*-1-*methyl*-2-*oxo*-1′-*phenylindolo*(3′ : 2′-3 : 4)*quinoline* (VIII) (0·25 g., 80%), colourless needles,

m. p. 218·5°, from acetone (Found : C, 81·7; H, 5·1; N, 9·0. $C_{22}H_{16}ON_2$ requires C, 81·5; H, 5·0; N, 8·65%). The oxidation also occurred in cold acetone solution, but the product (VIII) was then difficult to free from unchanged material.

The oxo-indole (VIII) is very weakly basic : in ethanolic solution it formed a picrate, pale orange needles, which partly dissociated on attempted recrystallisation.

1 : 2 : 3 : 4-*Tetrahydro*-1-*methyl*-4-*oxoquinoline methylphenylhydrazone*, similarly prepared to the diphenyl analogue, formed bright yellow crystals, m. p. 78—79°, from aqueous ethanol (Found : C, 77·2; H, 7·3; N, 15·9. $C_{17}H_{19}N_3$ requires C, 76·95; H, 7·2; N, 15·85%) : its indolisation was not investigated.

1 : 2-*Dihydro*-1-*methylquinolino*(3′ : 2′-3 : 4)*quinoline*-4′-*carboxylic Acid* (IX).—A solution of the crude ketone (IV) (3 g.) in ethanol (20 c.c.) and water (5 c.c.), to which isatin (3 g.) and potassium hydroxide (3·6 g.) were added, was boiled under reflux in nitrogen for 9 hr., cooled, filtered into 10% aqueous acetic acid (100 c.c.) and set aside overnight. The finely divided precipitated scarlet *acid* (IX) (5 g.) when collected, washed with much water and ethanol, and dried, had m. p. 172° (effervescence) (E.T., I.T. 160°) before and after heating at 60°/0·1 mm. for 5 hr., but was still impure (Found : C, 73·4; H, 5·1. Calc. for $C_{18}H_{14}O_2N_2$: C, 74·5; H, 4·9%). The acid is almost insoluble in all the usual liquids, but a small quantity, recrystallised from boiling acetic acid by using a filter-stick immersed in the heated solvent vapour, and then dried at 60°/0·1 mm. for 6 hr., had m. p. 175° (E.T., I.T. 160°); nevertheless it still retained acetic acid (Found : C, 72·8; H, 5·0; N, 9·5. $C_{18}H_{14}O_2N_2,0{\cdot}25C_2H_4O_2$ requires C, 72·8; H, 4·95; N, 9·2%); stronger heating was not practicable without risk of decarboxylation. The presence of this solvent prevented detection of an ·NH· band in the infra-red spectrum.

The crystals of the acid were apparently stable in air, and after one week showed no darkening, unlike the phenyl analogue (cf. Part I). The acid readily dissolved in concentrated aqueous potassium hydroxide or carbonate to give a yellow solution, but the potassium salt (XI) was isolated only as an uncrystallisable yellow gum.

The preparation and properties of the hydrochlorides of this acid will be described after those of the amines.

The Yellow Base (X).—The powdered acid (IX) (2 g.) was heated in a glass tube (3 cm. in diameter) at 180° rising to 230°/0·01 mm. for 1 hr., during which a straw-coloured liquid distilled and formed a viscous glass. The latter was removed under nitrogen and dissolved in boiling ethanol to which a small amount of water was then added; cooling deposited 1 : 2-*dihydro*-1-*methylquinolino*(3′ : 2′-3 : 4)*quinoline* (X) (1·25 g., 74%), vivid yellow crystals, m. p. 98—100° (E.T., I.T. 95°) after further recrystallisation from aqueous ethanol (Found : C, 82·9; H, 6·1; N, 11·5%; *M*, 239. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·75; N, 11·4%; *M*, 246). In ethanol or acetone, the base gives a bright yellow solution with a greenish-yellow fluorescence. The crystals apparently undergo slow oxidation in air, without change of colour : a sample so exposed for 48 hr. had m. p. 95·5—100° (E.T., I.T. 93°).

Action of Hydrogen Chloride on the Yellow Base (X).—(*A*) A stream of dry hydrogen chloride was passed into a dilute solution of the base in acetone; the bright yellow colour changed rapidly to deep red, which then faded until the solution was colourless. Addition of ether precipitated fine colourless needles, undoubtedly of the dihydrochloride, which, however, on removal from the acid solution rapidly dissociated and became deep red.

(*B*) Just sufficient hydrogen chloride was passed into a more concentrated acetone solution of the base to precipitate a mass of deep reddish-purple needles of the *monohydrochloride* (XII), m. p. 240—245° (E.T.) after crystallisation from acetone containing *ca.* 5% of ethanol (Found : C, 72·0; H, 5·4; N, 9·7. $C_{17}H_{14}N_2,HCl$ requires C, 72·2; H, 5·35; N, 9·9%). Heating caused the colour of the compound to show the changes : dark green (*ca.* 140°) ⟶ olive-green ⟶ greenish-yellow (*ca.* 200°). The finely powdered salt on exposure to the air passed slowly through the same changes and after 72 hr. had become yellow; in a vacuum the salt was stable indefinitely. A solution of the salt (XII) when treated with aqueous sodium hydroxide regenerated the base (X). The infra-red spectrum of the salt shows rather complex absorption at 3—4 μ, the main bands occurring at 3·6 and 3·85 μ.

The yellow base dissolves in concentrated hydrochloric acid to give a colourless solution, which on dilution immediately becomes reddish-purple.

The base gave a *monopicrate*, deep purple-red needles, m. p. 233° (decomp.), from aqueous ethanol (Found : C, 58·3; H, 3·7; N, 14·4. $C_{17}H_{14}N_2,C_6H_3O_7N_3$ requires C, 58·1; H, 3·6; N, 14·7%); this is stable at 70°, but at *ca.* 160° becomes dark olive-green, and darkens considerably from 220° to 233°.

A dilute red solution of the base in hydrochloric acid when treated with dilute aqueous

chloroplatinic acid deposited a deep red chloroplatinate, which on being heated became green and finally greenish-yellow, like the monohydrochloride. A colourless solution of the base in concentrated hydrochloric acid, treated with highly concentrated chloroplatinic acid, deposited a colourless amorphous *chloroplatinate*, which was collected, washed with hydrochloric acid, and dried in a vacuum (Found: C, 30·2; H, 2·6; Pt, 30·1. $C_{17}H_{14}N_2,H_2PtCl_6$ requires C, 31·1; H, 2·45; Pt, 29·8%). The salt rapidly became red in contact with hot solvents. The *di(chloroaurate)*, similarly prepared and isolated, formed a very pale yellow powder (Found: C, 21·9; H, 1·8; Au, 43·0. $C_{17}H_{14}N_2,2HCl_4Au$ requires C, 22·05; H, 1·75; Au, 42·6%), m. p. 235—240° (decomp.); in dilute solution, a red salt was obtained, and underwent the usual colour changes on heating.

A solution of the yellow base in methanolic methyl iodide, when heated, acquired an orange-red colour, but boiling under reflux in nitrogen for 4 hr. followed by concentration furnished the unchanged base. The base was also recovered unchanged when its ethanolic solution was boiled under reflux in nitrogen for 2 hr. with (*a*) *p*-dimethylaminobenzaldehyde (1·24 mols.) and a trace of alkali, or (*b*) diphenylformamidine (1·25 mols.).

The Orange Base (XV).—A solution of the yellow base (X) (0·65 g.) in dilute hydrochloric acid (25 c.c.) was boiled under reflux in nitrogen for 15 min., the deep purple solution becoming reddish-orange and finally yellow with a pale green fluorescence. On cooling, yellow needles (0·73 g., 100%) of the monohydrochloride (XIV) of 1 : 4′-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline (XV) separated, and on recrystallisation from ethanol under nitrogen gave the *monohydrate* as bright yellow hygroscopic needles, m. p. 243·5—244·5° (decomp.) (E.T., I.T. 230°) (Found: C, 68·3; H, 5·9; N, 9·3. $C_{17}H_{14}N_2,HCl,H_2O$ requires C, 67·9; H, 5·7; N, 9·3%). The m. p. is markedly affected by the rate of heating.

When the above hot yellow solution was transferred under nitrogen to an excess of dilute aqueous sodium hydroxide, the mixture on cooling deposited the *base* (XV) (92%), which, recrystallised from acetone, formed bright orange plates, m. p. 155° (E.T., I.T. 130°) (Found: C, 82·5, 82·55; H, 5·85, 5·6; N, 11·2%; *M*, 240. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·75; N, 11·4%; *M*, 246). In organic solvents it gives orange solutions having a slight orange fluorescence. It gives a bright yellow solution in both dilute and concentrated hydrochloric acid, in marked contrast to the yellow base (X).

The above yellow monohydrochloride (XIV) was also obtained (*a*) by boiling a suspension of the purple monohydrochloride (XII) in water under nitrogen, the above colour changes again occurring, and (*b*) by warming the orange base with dilute hydrochloric acid.

The base (XV) gave a *monopicrate*, dull yellow needles, m. p. 230° (decomp.) (I.T. 225°), from aqueous acetone (Found: C, 58·4; H, 3·65; N, 14·8. $C_{17}H_{14}N_2,C_6H_3O_7N_3$ requires C, 58·1; H, 3·6; N, 14·7%).

Addition of a solution of the base (XV) to one of an excess of chloroauric acid, each in concentrated hydrochloric acid, deposited the monochloroaurate as an orange-brown amorphous powder, m. p. 205° (decomp., shrinking at 155—165°): it was too unstable for purification (Found: C, 33·2; H, 2·5; Au, 34·9. Calc. for $C_{17}H_{14}N_2,HCl_4Au$: C, 34·9; H, 2·6; Au, 33·6%).

Oxidation of the Yellow Base (X).—(*a*) A saturated acetone solution of potassium permanganate was added dropwise in slight excess to one of the base (0·4 g.) in cold acetone (25 c.c.), decolorisation of the permanganate and precipitation of manganese dioxide rapidly occurring. The mixture was shaken for 1 hr., colourless needles separating. The mixed precipitate was collected and extracted with boiling acetone (100 c.c.), and the extract added to the filtrate, which on concentration deposited 1 : 2-*dihydro*-1-*methyl*-2-*oxoquinolino*(3′ : 2′-3 : 4)*quinoline* (XVI) (0·35 g., 83%), very pale cream needles, m. p. 218°, from acetone (Found: C, 78·4; H, 4·8; N, 10·6. $C_{17}H_{12}ON_2$ requires C, 78·4; H, 4·65; N, 10·75%).

(*b*) A solution of the base (50 mg.) in benzene (25 c.c.) was exposed to the air for 7 days, evaporation losses being replaced daily. The initial fluorescence was rapidly lost and precipitation of a cream-coloured solid occurred within 12 hr. The solution was then allowed to evaporate completely and the residue, recrystallised from acetone, yielded the amide (XVI) in almost theoretical yield and of m. p. 216·5—217·5°, alone and mixed.

An acetone solution of the amide (XVI), when treated with an excess of ethanol saturated with hydrogen chloride, deposited the hydrated *hydrochloride* as bright orange-yellow needles, m. p. 217—218°, when collected, washed with much acetone and dried over calcium chloride (Found: C, 62·9; H, 4·9; N, 8·6. $C_{17}H_{12}ON_2,HCl,1·5H_2O$ requires C, 63·1; H, 5·0; N, 8·65%). The hydrochloride readily dissociated on attempted recrystallisation, or at 60°/0·1 mm.; its m. p. indicates that dissociation to the free base is complete before fusion. The picrate was too unstable for purification.

Oxidation of the Orange Base (XV).—This was performed with permanganate precisely as above, and yielded the oxo-compound (XVI), m. p. and mixed m. p. 217°. A solution of the base (XV) in benzene also gave the same product on exposure to air. There was no obvious difference in the speed of oxidation of the bases (X) and (XV) in benzene solution, unlike that of (I) and (II).

The base (XV) was stable in a desiccator for 14 days or a specimen-tube for 10 days (unchanged in colour and m. p.).

Conversion of the Base (XV) *into the Base* (X).—The orange base (XV) (50 mg.) was heated in a small sublimation tube at 200—230°/0·1 mm. Rapid distillation occurred, giving a straw-coloured glass, which was extracted with hot ethanol under nitrogen. The yellow extract, when diluted with a small amount of water and allowed to cool, deposited the highly crystalline bright yellow base (X), m. p. and mixed m. p. 96—98°.

The Isomerism of the Acid (IX) *and its Monohydrochloride* (XVII).—(*a*) When a mixture of the finely powdered acid (IX) and 20% hydrochloric acid was vigorously shaken, the latter immediately became intense purple in colour, and the acid (IX) was immediately transformed into the deep blackish-purple monohydrochloride (XVII), m. p. 170—172° (effervescence) (E.T.), the salt becoming reddish-brown before melting. The very low solubility of both the acid (IX) and the monohydrochloride (XVII), and the instability of the latter to heat, prevented the isolation of the salt free from traces of unchanged (IX) (Found: C, 68·8; H, 5·4; N, 9·0. Calc. for $C_{18}H_{14}O_2N_2$,HCl: C, 66·2; H, 4·65; N, 8·6%); the infra-red spectrum of (XVII) was therefore not investigated.

(*b*) The purple hydrochloride (XVII) was thoroughly ground with 20% hydrochloric acid, and the mixture then boiled under reflux in nitrogen for *ca.* 30 min., the colour of the liquid gradually fading to pale yellowish-brown as (XVII) completely dissolved and was replaced by the highly crystalline insoluble deep green *monohydrochloride*. A sample, when washed thoroughly with water and acetone and dried in a vacuum over phosphoric anhydride, had m. p. 250° (effervescence) (E.T., I.T. 230°) (Found: C, 66·1; H, 4·8; N, 8·9. $C_{18}H_{14}O_2N_2$,HCl requires C, 66·2; H, 4·65; N, 8·6%).

(*c*) When the boiling of the above mixture in (*b*) was continued for *ca.* 7 hr., the solution became very pale and the green crystals became dull yellow, remaining highly crystalline. The yellow *monohydrochloride* (XIX), collected as before, had m. p. 250° (effervescence) (E.T.) (Found: C, 66·4; H, 4·9; N, 8·9. $C_{18}H_{14}O_2N_2$,HCl requires C, 66·2; H, 4·65; N, 8·6%). The same salt was obtained when the pure green crystals were heated at 200°/0·01 mm. for 45 min.

(*d*) The green or the yellow monohydrochloride, when added to hot dilute aqueous sodium carbonate, gave a yellow solution which, on cooling, deposited the highly crystalline 1 : 4′-*dihydro*-1-*methylquinolino*(3′ : 2′-3 : 4)*quinoline*-4′-*carboxylic acid* (XX), yellow hygroscopic needles, m. p. 138° (E.T.) (effervescence, resolidifying and remelting at 205—220°), from water (Found: C, 74·3; H, 4·95; N, 9·9. $C_{18}H_{14}O_2N_2$ requires C, 74·4; H, 4·85; N, 9·7%). This acid forms a hydrate, which undergoes complete dehydration only on prolonged exposure in a vacuum to phosphoric anhydride [cf. the hydrochloride (XIV) of the corresponding base (XV)].

A solution of the acid (XX), or of either form of its monohydrochloride, in hot concentrated aqueous potassium hydroxide on cooling deposited the yellow hygroscopic potassium salt, which could not be obtained pure. The yellow sodium salt was similarly obtained.

Decarboxylation. (*a*) The green and the yellow monohydrochloride (XIX) of the acid (XX) ultimately behaved identically when heated up to 250—300°/0·003 mm., in a narrow tube, since the initial effect on the green salt was conversion into the yellow. The results are recorded on p. 386.

(*b*) The yellow acid (XX), when cautiously heated at 15 mm. in a similar tube, melted with effervescence and gave a distillate which condensed to a bright yellow glass, and on crystallisation from aqueous ethanol afforded the vivid yellow crystals of the yellow base (X), m. p. 97—99°, alone and mixed.

1 : 2-*Dihydroquinolino*(3′ : 2′-3 : 4)*quinoline*-4′-*carboxylic Acid* (as IX).—This acid was prepared as Clemo and Perkin direct, the alkaline reaction mixture being filtered into an excess of 10% aqueous acetic acid to precipitate the dull red microcrystalline acid (82%), which became bright yellow at 170—175° and melted at 185°: as Clemo and Perkin found, the acid could not be completely purified (Found: N, 9·4. Calc. for $C_{17}H_{12}O_2N_2$: N, 10·1%).

When a solution of this acid in hot hydrochloric acid was boiled, the purple-red colour soon faded and a pale yellow-buff precipitate (presumably of an unstable monohydrochloride) was deposited. The latter, recrystallised from a large volume of aqueous ethanol, afforded the yellow amorphous 1 : 4-*dihydroquinolino*(3′ : 2′-3 : 4)*quinoline*-4′-*carboxylic acid hemihydrate*,

m. p. 201° (effervescence) (E.T.) (Found: C, 71·9; H, 4·7; N, 9·7. $C_{17}H_{12}O_2N_2,0{\cdot}5H_2O$ requires C, 71·6; H, 4·6; N, 9·8%). The ultra-violet spectrum of this acid in aqueous 0·1N-sodium hydroxide solution shows the characteristics:

$\lambda_{max.}$	364—365	224	$\lambda_{min.}$	322—323	$\lambda_{inf.}$	324—329	246—250
$\varepsilon_{max.}$	7980	35,400	$\varepsilon_{min.}$	3990	$\varepsilon_{inf.}$	4000	21,800

The red acid, when heated at 190—200°/0·1 mm., gave a yellow crystalline sublimate (XXII*A* or *B*), which when recrystallised from aqueous ethanol, ground thoroughly with aqueous sodium hydroxide, washed, and resublimed, had m. p. 227—228° (softening at 225°) (Found: N, 12·4. Calc. for $C_{16}H_{12}N_2$: N, 12·1%). The ultra-violet spectra in (*A*) ethanol, (*B*) 0·1N-hydrochloric acid gave the values:

(*A*) $\lambda_{max.}$ ...	360—363	301	296	253	243	225				
$\varepsilon_{max.}$ ...	12,300	3,140	3,000	19,000	18,000	44,800				
$\lambda_{min.}$ ...	308	297	294	245	240	211				
$\varepsilon_{min.}$ ...	2,890	2,980	2,960	18,450	18,300	32,500				
(*B*) $\lambda_{max.}$ ...	390	247	226	$\lambda_{min.}$ ...	322	236	214—215	$\lambda_{inf.}$ ...	285—289	
$\varepsilon_{max.}$ ...	14,300	21,200	37,400	$\varepsilon_{min.}$ ...	1,180	16,100	18,600	$\varepsilon_{inf.}$ ...	5130	

The yellow base in hot hydrochloric acid gave a yellow solution with a greenish fluorescence, and on cooling deposited the *monohydrochloride*, bright yellow needles, m. p. 310—312° (decomp., softening at *ca.* 305°) (E.T.), after crystallisation from aqueous ethanol (Found: N, 10·3. $C_{14}H_{13}N_2,HCl$ requires N, 10·4%). Prolonged boiling of the above solution caused no colour change, and cooling and rendering alkaline precipitated the unchanged base. The latter shows no tendency to form a colourless solution in a large excess of cold concentrated hydrochloric acid: in this respect it resembles the orange base (XV) and differs strikingly from the yellow base (X).

Isomerism in the 1-Phenyl Series.—(i) A solution of the yellow 1-phenyl base (as X) in concentrated hydrochloric acid was boiled for 15 min., but the deep red colour remained unchanged, and the solution on cooling deposited the deep red crystalline monohydrochloride (as XII), m. p. 280° (decomp.) (cf. Part I). (ii) This solution was boiled under reflux for 6 hr.; the change in colour to yellowish-brown then appeared complete. The solution, on cooling, deposited the isomeric yellow crystalline *monohydrochloride* (as XIV), m. p. 228—230° (decomp.) (E.T.) (Found: N, 8·15. $C_{32}H_{16}N_2,HCl$ requires N, 8·1%). This salt on treatment with aqueous sodium hydroxide yielded a dull orange base, but insufficient material precluded purification and investigation.

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 20th*, 1954.]

The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part VII. Derivatives of* 1 : 6-*Dioxojulolidine.*†

By JOHN T. BRAUNHOLTZ and FREDERICK G. MANN.

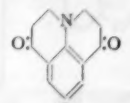
[Reprint Order No. 5671.]

The bisphenyl- and bisdiphenyl-hydrazones of 1 : 6-dioxojulolidine undergo the Fischer indolisation to furnish the corresponding di-indolo-julines; the first of these is stable only as its salts. ψ-Indole formation was not observed in this series.

1 : 6-Dioxojulolidine, when submitted to the Pfitzinger reaction with isatin, gives the purple diquinolinojulinedicarboxylic acid (IV), which on heating undergoes the allylic rearrangement to the orange isomeric acid (V). The latter on decarboxylation gives the orange diquinolino-juline (VI), which when heated with hydrochloric acid shows the same rearrangement, with formation of the isomeric red base (VII); sublimation reconverts (VII) into (VI).

AN examination has been made, on closely similar lines to the work described in Part VI,* of the product obtained when (*a*) the bisphenylhydrazone of 1 : 6-dioxojulolidine (I) is subjected to the Fischer indolisation, and (*b*) the base (I) is condensed by the Pfitzinger reaction with isatin in alkaline solution. The possible isomerisation of the products obtained by the Pfitzinger reaction has also been studied, but the far greater insolubility of these products and their duplication of chemical function has prevented so exhaustive a study of their derivatives as that on the products described in Part VI.

When a solution of the bisphenylhydrazone of 1 : 6-dioxojulolidine (I) in ethanolic hydrogen chloride was boiled, the initial deep purple colour slowly faded to orange, and the highly crystalline orange monohydrochloride of di-indolo(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)juline



(I)

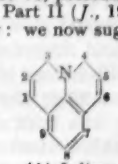
(II)

(III)

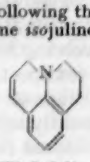
(II; R = H) separated; this salt was converted into the crystalline orange monohydriodide, thiocyanate, and picrate, and it is clear that in these compounds salt formation (as expected) has occurred on the central nitrogen atom. Treatment of a solution of the hydrochloride with aqueous sodium hydroxide precipitated the di-indolo-compound (II; R = H) as a lemon-yellow flocculent mass, which on exposure to light and air underwent rapid darkening, so that purification and spectroscopic examination were not possible. In view of the results obtained with 1-oxojulolidine (Mann and Smith, *J.*, 1951, 1898), and with 1 : 2 : 3 : 4-tetrahydro-4-oxo-1-phenylquinoline (Mann, *J.*, 1949, 2816) and its 1-methyl analogue (Part VI), it might have been expected that the above indolisation would have been accompanied by dehydrogenation and the formation of the dehydro-derivative (III). Evidence that salts of the true indole (II; R = H) have been formed is provided by analysis, and by the strong probability, based on previous examples, that the colour of a ψ-indole such as (III) would be markedly more intense than that of its salts. Furthermore, the indolisation of the bisdiphenylhydrazone of (I) similarly gave

* Part VI, preceding paper.

† In Part II (*J.*, 1951, 1898), following the Editor's advice, the bases (A), (B), and (C) were named as below: we now suggest the name *iso*juline for (D).



(A) Juline



(B) Juloline

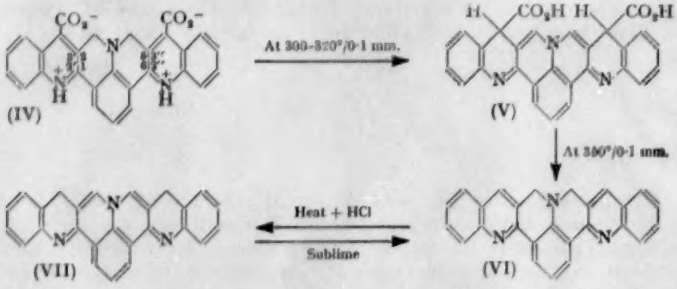
(C) Julolidine

(D) *iso*Juline

the orange crystalline monohydrochloride of 1′ : 1″-diphenyldi-indolo(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)juline (II; R = Ph); in this case the pure di-indolo-compound (II; R = Ph) could be isolated, but it rapidly decomposed when in contact with organic solvents.

The reason why in this series the true indole (II), and not the *ψ*-indole (III), is formed remains uncertain. It may be significant that the *ψ*-indoles previously described have been strong anhydronium bases, giving stable salts in which the whole cation had become fully aromatic in structure: this process would not be possible in (III) because of the central nitrogen atom.

When a solution of the diketone (I) and isatin in aqueous methanolic sodium hydroxide was boiled for twenty hours, filtration of the orange liquid into dilute acetic acid caused deposition of fine deep purple crystals of diquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)juline-4′ : 4″-dicarboxylic acid (IV). The evidence for the zwitterion structure (IV) is: (i) This resonance structure would receive contributions from numerous canonical forms, in which any two of the three nitrogen atoms can accept the protons; hence it would certainly be intensely coloured. (ii) The acid dissolves in hydrochloric acid to give a blackish-purple solution, but dissolves in sodium hydroxide to give an orange solution and ultimately a hygroscopic crystalline yellow salt; clearly the hydrochloric acid would convert the $\cdot CO_2^-$ ions in (IV) into $\cdot CO_2H$ groups, without affecting the fundamental structure or colour, whereas alkalis would remove the proton from the nitrogen atoms in (IV) and thus destroy resonance of the above type. (iii) The infra-red spectrum of (IV) is ill-defined in the 3-μ region, with peaks at 2·95 and 3·13 μ, but two strong bands appear at 6·20 and 6·35 μ, the latter being the stronger and sharper. Amino-acids having a zwitterion structure usually have a band at 6·11—6·21 μ and a stronger one at 6·21—6·38 μ. The peaks in the 3-μ region and the band at 6·35 μ in the spectrum of (IV) can therefore be ascribed to the $\equiv NH^+$ and the $\cdot CO_2^-$ groups, respectively.



The acid (IV) was recovered unchanged after several hours' boiling with hydrochloric acid. When, however, the powdered acid was cautiously heated to 300—320°/0·1 mm., *i.e.*, well below its decomposition temperature, it became bright orange without change in composition. This transformation is apparently due to " allylic rearrangement " (cf. Part VI) and the consequent formation of 4′ : 4″-dihydrodiquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*iso*juline-4′ : 4″-dicarboxylic acid (V). The evidence for this structure is: (i) The acid (V) dissolves in aqueous sodium hydroxide solution to give a yellow solution, the ultra-violet spectrum of which is markedly different from that of a similar solution of the acid (IV) (p. 397); the two acids are therefore structurally distinct. (ii) The alkaline solution of (V) when poured into an excess of acetic acid gives a blood-red colour markedly different from the intense purple colour which the acid (IV) shows under these conditions; proton addition to the 1′ : 1″-nitrogen atoms in (V) would give a cation showing a resonance similar to that of (IV) but involving fewer quinonoid rings and hence presumably causing less intense colour. The infra-red spectrum is also ill-defined in the 3-μ region, with peaks at 3·02 μ and 3·12 μ, but shows a single strong band at 6·35 μ; the weaker band at 6·11—6·21 μ shown by amino-acids is apparently indicated only as a faint shoulder at 6·20 μ whereas the band at 5·85 μ shown by un-ionised carboxylic acids is absent. The position of the protons in the acid (V) is therefore uncertain: the infra-red evidence on

the whole indicates a zwitterion structure, which is not supported by the marked colour change caused by acidification. The apparent contradiction may be due to intermolecular hydrogen bonding or (less probably) to some influence exerted by the central nitrogen atom. The spectroscopic evidence however places the structural difference of the acids (IV) and (V) beyond doubt.

Although the allylic rearrangement in compounds of this general type is usually promoted by hot acids, the above thermal transformation is strictly comparable to that of 1 : 2-dihydroquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid (Part VI, *loc. cit.*).

The acid (IV), when more vigorously heated under reduced pressure, was first converted into the acid (V), which then underwent decarboxylation and gave a crystalline orange sublimate. This dissolved in hot pyridine to form an orange solution which had a vivid yellow fluorescence, and which on cooling deposited diquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)juline (VI) in deep orange needles, m. p. 319°. This base dissolved in hot concentrated

FIG. 1.

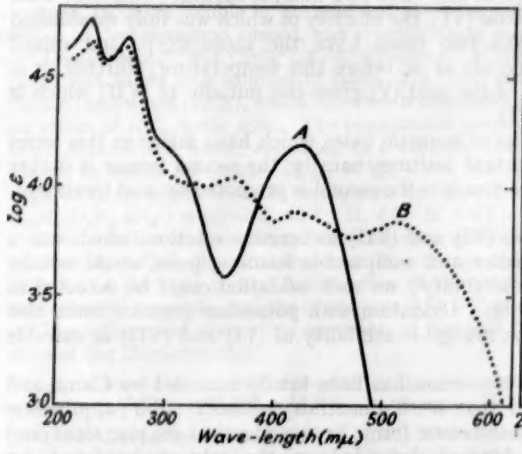


FIG. 2.

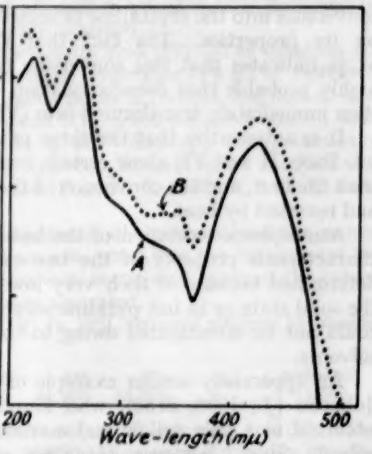


FIG. 1. *Diquinolino*(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*juline* (VI), (*A*) *in methanol* (1·20 *mg.*/250 *c.c.*); (*B*) *in methanol* (1·30 *mg.*/200 *c.c.*) *containing* 0·25 *c.c. of* 3N-HCl.

FIG. 2. 4′ : 4″-*Dihydrodiquinolino*(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*isojuline* (VII), (*A*) *in methanol* (0·77 *mg.*/50 *c.c.*); (*B*) *in methanol* (0·77 *mg.*/50 *c.c.*) *containing* 0·30 *c.c. of* 3N-HCl.

hydrochloric acid to form a purple solution very similar in colour to a solution of the acid (IV); this solution deposited purple crystals of a hydrochloride, stable only in presence of hydrochloric acid. The purple colour indicates that the cation of the hydrochloride has the same essential structure as (IV), with of course the $\cdot CO_2^-$ groups replaced by hydrogen atoms; this cation will therefore show similar resonance. This is confirmed by the ultra-violet absorption spectra (Fig. 1) of the base (VI) in methanol and in methanolic hydrochloric acid: the marked difference in these spectra demonstrates the considerable (resonance) difference in the base and its hydrochloride.

It is clear therefore that heating the acid (IV) involves the allylic rearrangement to (V), with a reversal of this process as the decarboxylated product volatilises (see below).

When the purple solution of the base (VI) in concentrated hydrochloric acid was boiled under reflux, a very slow colour change occurred, and ultimately the solution became deep reddish-brown and a brown crystalline hydrochloride separated. This salt was also unstable in the absence of an excess of acid, but when treated with aqueous sodium hydroxide gave an isomeric base (VII), which crystallised from pyridine in dark red needles, m. p. 319°, alone or when mixed with (VI).

The fact that the bases (VI) and (VII) are isomeric and are not dimorphic forms of the same compound is based on the following evidence. (i) The deep orange and the deep

red colour of the bases, shown by crystals of approximately the same size, is retained when the crystals are very finely ground; the colours are thus the true colours of the bases and are not due to surface reflexion (cf. Part VI). (ii) The base (VII) in hot pyridine gives a deep red solution with a faint orange-red fluorescence, and in warm concentrated hydrochloric acid a pale yellowish-brown solution. (iii) The ultra-violet absorption spectra of (VII) in methanol and in methanolic hydrochloric acid (Fig. 2) are closely similar, indicating that salt formation has made no significant change in the structure. (iv) The infra-red spectra of (VI) and (VII) are unlike (p. 397).

It is therefore almost certain that the hydrochloric acid has again caused the allylic rearrangement, and that the dark red base is 4′ : 4″-dihydrodiquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*iso*juline (VII), and that salt formation occurs solely on the central nitrogen atom. There is of course no evidence as to whether the allylic rearrangement occurs on one or both sides of the molecule, and the symmetric double rearrangement has been assumed; this is the logical conclusion if the mechanism suggested in Part VI is correct.

When the red base (VII) was heated at 280—300°/0·1 mm., it sublimed smoothly with conversion into the crystalline orange base (VI), the identity of which was fully established by its properties. The fact that the two bases have the same m. p. and mixed m. p. indicates that this conversion occurs at or before this temperature; further, it is highly probable that decarboxylation of the acid (V) gives rise initially to (VII) which is then immediately transformed into (VI).

It is noteworthy that the three pairs of isomeric bases which have arisen in this series (cf. Parts II and VI) show certain constant features, namely, the second isomer is darker than the first, and the conversion of the first into the second is promoted by acid treatment, and reversed by heat.

Atmospheric oxidation of the bases (VI) and (VII) in benzene solution, which was a characteristic property of the two earlier and comparable isomeric pairs, could not be determined because of their very low solubility; no such oxidation could be detected in the solid state or in hot pyridine solution. Oxidation with potassium permanganate also could not be investigated owing to the negligible solubility of (VI) and (VII) in suitable solvents.

An apparently similar example of isomerism has been briefly recorded by Clemo and Johnson (*J.*, 1930, 2133), who found that 5′ : 6′-dimethoxyindeno(2′ : 3′-3 : 4)quinoline occurred in a pale yellow and a reddish-brown form, having identical m. p.s, alone and mixed. Since, however, the form obtained depended on the solvent employed for crystallisation, and the fluorescent properties of their solutions were apparently identical, dimorphism cannot be excluded.

Experimental

M. p.s, unless otherwise recorded, were determined in evacuated sealed tubes, which were immersed at 10—15° below the m. p.

Di-indolo(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*juline* (II; R = H).—The bisphenylhydrazone of 1 : 6-dioxojulolidine (1 g.) (Mann and Smith, *loc. cit.*) was dissolved in saturated ethanolic hydrogen chloride (40 c.c.), to which ethanol (10 c.c.) had been added, and the purple solution boiled under reflux for 5 hr., its colour changing meanwhile to orange and crystals being deposited. It was set aside overnight, and the orange crystalline monohydrated *monohydrochloride* of the di-indolojuline (II; R = H), when then collected and thoroughly washed with warm water, had m. p. 346° (decomp.) (yield, 0·6 g., 57%) (Found: C, 71·8; H, 4·8; N, 10·6. $C_{24}H_{17}N_3$,HCl,H_2O requires C, 71·75; H, 5·0; N, 10·45%). The salt is too insoluble for recrystallisation.

A solution of the hydrochloride in boiling methanol, when added to a similar solution of sodium iodide, precipitated the *monohydriodide*, m. p. above 400° (Found: C, 60·5; H, 3·5; N, 8·65. $C_{24}H_{17}N_3$,HI requires C, 60·65; H, 3·8; N, 8·85%). The *thiocyanate*, similarly prepared by using potassium thiocyanate, formed a microcrystalline powder, m. p. 318° (decomp.) (Found: C, 73·6; H, 4·3; N, 13·6. $C_{24}H_{17}N_3$,HCNS requires C, 73·85; H, 4·45; N, 13·8%). The *monopicrate* had m. p. 253° (decomp.) (Found: C, 62·3; H, 3·35; N, 14·3. $C_{24}H_{17}N_3$,$C_6H_3O_7N_3$ requires C, 62·5; H, 3·5; N, 14·55%). All these salts separated as bright orange crystals.

A solution of the monohydrochloride in much boiling aqueous methanol was filtered into an

excess of 10% aqueous sodium hydroxide, and the precipitated lemon-yellow base (II; R = H) collected and washed as rapidly as possible. Its colour began to deepen almost immediately when it was exposed to light and to air, and more slowly in a vacuum. The base recrystallised from acetone–ethanol as yellow platelets, but these could not be isolated free from the decomposition product.

1′ : 1″-*Diphenyldi-indolo*(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*juline* (II; R = Ph).—The bisdiphenylhydrazone of (I) (Braunholtz and Mann, *J.*, 1953, 1823), when treated as above, also ultimately gave a pale orange solution containing ammonium chloride crystals. The filtered solution, when concentrated, diluted with water, and set aside overnight, deposited the *monohydrochloride* of the juline (II; R = Ph), bright orange crystals, m. p. 260° (decomp.), from aqueous ethanol (Found: C, 80·8; H, 5·3; N, 7·75. $C_{36}H_{25}N_3$,HCl requires C, 80·65; H, 4·9; N, 7·8%). This salt when added to aqueous sodium hydroxide (as above) precipitated the *juline* (II; R = Ph), which when thoroughly washed with water and ethanol and dried at 65°/0·1 mm. formed a mustard-coloured amorphous powder, m. p. 170° (decomp.) (Found: N, 8·5. $C_{36}H_{25}N_3$ requires N, 8·4%). The base, when heated at 0·01 mm., underwent fusion and then charring, without detectable sublimation. It was sparingly soluble in hot ethanol and acetone, far more soluble in benzene and pyridine, but all such solutions rapidly darkened in colour as decomposition ensued, and crystallisation was not achieved.

Diquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*juline*-4′ : 4″-*dicarboxylic Acid* (IV).—The diketone (I) (2 g.) was added to a solution of isatin (3 g.) and potassium hydroxide (3·6 g.) in methanol (25 c.c.) and water (5 c.c.), which was then boiled under reflux for 20 hr., cooled, and filtered into an excess of 10% acetic acid. The precipitated purple acid (IV), when collected, washed with much ethanol and water, and dried in a vacuum, had m. p. 363° (decomp., with preliminary change in colour to orange) (4 g., 87%). The acid is hygroscopic, and before analysis was exposed to air until the stable *tetrahydrate* had been formed (Found: C, 63·2; H, 4·9; N, 7·65. $C_{32}H_{17}O_4N_3$,4H_2O requires C, 63·2; H, 4·7; N, 7·9%).

The acid dissolved readily in warm aqueous sodium hydroxide or carbonate, and the orange solution on cooling deposited the crystalline orange sodium salt, which was too deliquescent for isolation in the pure state. Acidification of the solution with acetic acid changed the colour immediately to purple, and the crystalline acid (IV) slowly separated.

The ultra-violet absorption spectrum of the acid (IV) in 10% aqueous sodium hydroxide showed the characteristics:

$\lambda_{max.}$	... 390—393	266	229—231	$\lambda_{min.}$	... 356	252	224	$\lambda_{infl.}$	... 300—308
$\varepsilon_{max.}$	... 10,950	46,600	58,900	$\varepsilon_{min.}$	... 7050	40,800	56,000	$\varepsilon_{infl.}$	... 14,600

4′ : 4″-*Dihydroquinolino*(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)iso*juline*-4′ : 4″-*dicarboxylic Acid* (V).—The finely powdered acid (IV) was cautiously heated at 300—320°/0·1 mm. until conversion into the orange acid (V) was complete. This acid is also hygroscopic, and when exposed to the air for 12 hr. became brown, the change being reversed by gentle warming under reduced pressure. A sample of the freshly prepared acid, exposed to the air but analysed before the onset of darkening, had formed a *sesquihydrate* (Found: C, 68·9; H, 4·3; N, 8·9. $C_{34}H_{17}O_4N_3$,1·5H_2O requires C, 69·2; H, 4·15; N, 8·65%). The anhydrous acid had m. p. 363° (decomp.), showing that in a normal m. p. determination the conversion (IV) ⟶ (V) is complete before fusion.

A solution of (V) in aqueous 10% sodium hydroxide was too dilute for accurate determination of ε values, but showed the characteristics: $\lambda_{max.}$ 424—428, $\lambda_{min.}$ 412—414, $\lambda_{infl.}$ 438—456, 376—388.

Diquinolino(2′ : 3′-1 : 2)(3″ : 2″-5 : 6)*juline* (VI).—The preparation of this compound was best carried out by heating the purple acid (IV) in a cold-finger sublimation apparatus, at first gently at 15 mm. to ensure dehydration and conversion into (V) and then in a metal-bath at *ca.* 350°/0·1 mm.; decarboxylation then occurred with deposition of a crystalline sublimate, which was yellow to orange according to the particle size. The sublimate, recrystallised from pyridine, gave the *juline* (VI), lustrous deep orange needles, m. p. 319·5° (decomp.) (Found: C, 84·3; H, 4·7; N, 11·15. $C_{34}H_{17}N_3$ requires C, 84·1; H, 4·6; N, 11·3%); the low yield (50%) was due to extensive charring at the decarboxylation temperature.

The infra-red spectrum of (VI) shows in particular a sharp band at 6·23 μ flanked by weaker bands at 6·15 and 6·33 μ, and a strong single band at 13·55 μ.

The purple solution of the juline (VI) in hot concentrated hydrochloric acid, on cooling, deposited an unstable deep bluish-purple crystalline hydrochloride, which when collected and washed with water became red and finally yellow; this colour change also occurred when the hydrochloride, after being washed with hydrochloric acid, was dried in a vacuum.

4 : 4''-*Dihydroquinolino*(2' : 3'-1 : 2)(3'' : 2''-5 : 6)iso*juline* (VII).—A solution of the base (VI) in concentrated hydrochloric acid was boiled under reflux for 4 hr., the deep purple colour becoming slowly reddish and finally yellowish-brown, and a reddish-brown crystalline hydrochloride separating from the boiling solution. A sample of this hydrochloride when collected and exposed to the air became olive-green and when warmed with water became yellowish-brown; purification was therefore not attempted. When the cold reaction mixture was treated with aqueous sodium hydroxide, the particles of the hydrochloride became at first yellowish and then dull red. The crude base, when collected and recrystallised from pyridine, furnished the iso*juline* (VII) as lustrous deep red needles, m. p. 319° (Found : C, 83·9; H, 4·9; N, 11·5. $C_{26}H_{17}N_3$ requires C, 84·1; H, 4·6; N, 11·3%); the yield was almost quantitative.

The main features of the infra-red spectrum of (VII) are bands at 6·07, 6·15, and 6·25 μ (of strength, 6·07 > 6·25 > 6·15) and a strong broad-based band at 13·38 μ flanked by weaker bands at 13·1 and 13·8 μ (cf. VI).

Conversion of the Base (VII) *into the Isomer* (VI).—The red base (VII) (150 mg.), when heated in a small sublimation apparatus at 280—300°/0·1 mm., gave the beautifully crystalline deep orange base (VI) (140—150 mg.), which was identified by its m. p., infra-red spectrum, and the colour of solutions in organic solvents and in hydrochloric acid.

We are indebted to Imperial Chemical Industries Limited, Dyestuffs Division, for the gift of intermediate chemicals.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 20th,* 1954.]

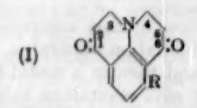
Cyanine Dyes derived from 1 : 6-*Dioxojulolidine.*

By JOHN T. BRAUNHOLTZ and FREDERICK G. MANN.

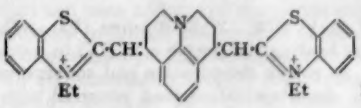
[Reprint Order No. 5672.]

7-Methyl-1 : 6-dioxojulolidine condenses with 2-methylbenzothiazole ethiodide to give the cyanine iodide (III), but the corresponding derivative could not be obtained from 1 : 6-dioxojuloline. The latter readily condenses with *p*-dimethylaminobenzaldehyde and *p*-nitrosodimethylaniline to give *mero*cyanines of type (IV). Other derivatives are briefly described.

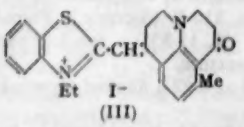
We have attempted to condense both carbonyl groups in 1 : 6-dioxojulolidine (I; R = H) with the reactive methyl groups of 2-methylbenzothiazole ethiodide, quinaldine ethiodide, and lepidine ethiodide, since this condensation would produce a very interesting type of cyanine dye [for example, (II)] in which any two of the three nitrogen atoms could accept the positive charges. These attempts, using either (I; R = H) or its 7-methyl homologue (I; R = Me), failed to produce crystalline products of the desired type, although the intense colour of the reaction mixture indicated some condensation. The condensation of (I; R = Me) with 2-methylbenzothiazole ethiodide in boiling pyridine did however produce [2-(3-ethylbenzothiazole)][1-(7-methyl-6-oxojulolidine)]methincyanine iodide (III),



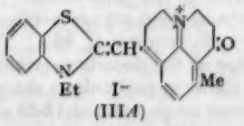
(I)



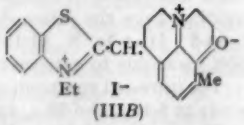
(II)



(III)



(III*A*)



(III*B*)

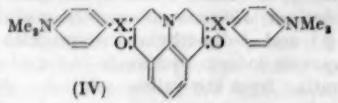
brownish-red needles giving a reddish-purple solution in methanol. The reason why (I; R = Me) condenses with one but not two equivalents of the ethiodide whilst (I; R = H) gives no satisfactory condensation is obscure. Hyperconjugation between a nuclear

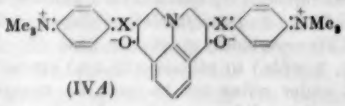
methyl group and a ·CO·CH_2· system may increase the activity of the ketone by causing increased enolisation (Cardwell and Kilner, *J.*, 1951, 2430); this increased activity in (I; R = Me) might be transmitted to either carbonyl group, and the structure (III) has been adopted solely because no steric hindrance occurs at the 1-keto-group. The compound (III) is a true cyanine dye in that the form (III*A*) will contribute to the salt, with, however, additional contribution by the *mero*cyanine form (III*B*). The compound (III) has certain structural resemblances to cyanine dyes containing the pyrrocoline nucleus (Holliman and Schickerling, *J.*, 1951, 914).

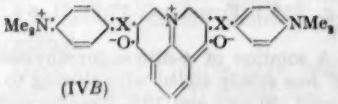
An entirely different type of *mero*cyanine has been obtained by the condensation of (I; R = H) with *p*-dimethylaminobenzaldehyde to give [2 : 5-(1 : 6-dioxojulolidine)][bis-4-(dimethylaminobenzene)]bismonomethin*mero*cyanine (IV; X = CH), orange needles giving a yellow solution in dioxan, and with *p*-nitrosodimethylaniline to give [2 : 5-(1 : 6-dioxojulolidine)][di-4-(dimethylaminobenzene)]dimonoazamethin*mero*cyanine (IV; X = N), bluish-purple needles giving a purple solution in acetone. Each of these compounds will receive contributions from the forms (IV), (IV*A*), and (IV*B*).

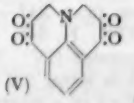
Tests carried out by Imperial Chemical Industries Limited, Dyestuffs Division, show that the dye (III) has a moderate sensitising action over the range 460—610 mμ, but that the *mero*cyanines (IV; X = CH) and (IV; X = N) have none (cf. p. 401).

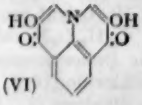
The acid hydrolysis of the *mero*cyanine (IV; X = N) was performed in order to prepare 1 : 2 : 5 : 6-tetraoxojulolidine (V). The brown highly crystalline product, having the composition of (V), was insoluble in all organic solvents except boiling nitrobenzene, would not condense with *o*-phenylenediamine, and dissolved in aqueous sodium hydroxide to form an intensely purple solution. These properties strongly indicate that the


(IV)


(IV*A*)

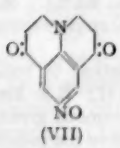

(IV*B*)

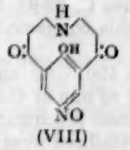

(V)

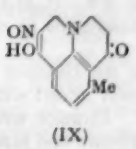

(VI)

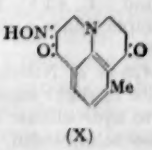
tetraketone (V) undergoes dienolisation to 2 : 5-dihydroxy-1 : 6-dioxo*iso*juline (VI), which in turn undergoes intermolecular hydrogen bonding; this suggestion is supported by the infra-red spectrum of the crystals, which shows strong sharp bands at 3·05 and 6·01 μ, the former corresponding to a hydrogen-bonded hydroxyl group and the latter to the carbonyl group.

The action of nitrous acid on the system (I) may be briefly recorded. We have attempted to convert (I; R = H) into the 8-nitroso-derivative (VII), in the hope that the action of hot aqueous alkalis would then give the *meta*-bridged derivative (VIII). The compound


(VII)


(VIII)


(IX)


(X)

(I; R = H) resisted nitrosation, but the 7-methyl derivative gave a crystalline mustard-coloured mononitroso-compound, m. p. 156°, soluble in organic solvents. This product, when treated with aqueous sodium hydroxide, or even when subjected to excessive heating during recrystallisation, was converted into a dark brown solid, m. p. 158°, of the same composition, but insoluble in all the usual solvents. There is at present no evidence for the structure of these two products. In view, however, of the known activation of one

ketone group in the dioxo-base (I; R = Me) by the 7-methyl group, it is possible that the initial crystalline derivative is 1-hydroxy-7-methyl-2-nitroso-6-oxojuloline (IX), and that the action of alkali gives the hydroxyimino-compound (X), possibly followed by a Beckmann rearrangement to a seven-membered cyclic acid amide. The remarkable stability of 1 : 6-bishydroxyiminojulolidine has already been described (Braunholtz and Mann, *J.*, 1952, 3046).

Experimental

Certain m. p.s, denoted by (E. T.), were determined in evacuated sealed tubes.

When solutions of the diketone (I; R = H) and 2-methylbenzothiazole ethiodide (1 or 2 mols.) in pyridine, piperidine, or methanolic triethylamine were boiled under reflux for 10—20 hr., evaporation of the intensely red solution gave the unchanged compounds with traces of a deep red gum. Similar results were obtained when the ethiodides of quinaldine and lepidine were employed.

[2-(3-*Ethylbenzothiazole*)][1-(7-*methyl*-6-*oxojulolidine*)]*methincyanine Iodide* (III).—A solution of the base (I; R = Me) (220 mg.) and 2-methylbenzothiazole ethiodide (310 mg., 1 mol.) in pyridine (5 c.c.) was boiled under reflux for 10 hr. A red solid separated on cooling, and a second crop was obtained by concentration. The combined crops were washed with much hot water and ethanol, and then crystallised from methanol, giving the brownish-red monohydrated *iodide* (III), m. p. 288° (decomp.) (Found: C, 53·4; H, 4·75; N, 5·3. $C_{28}H_{23}ON_2IS,H_2O$ requires C, 53·2; H, 4·8; N, 5·3%). The use of the ethiodide (2 mols.) and 15 hours' heating increased the yield from 11% to 17%.

No dye could be isolated when the pyridine in the above experiment was replaced by methanol containing piperidine or 10% aqueous sodium hydroxide, or when the quaternary salt was replaced by quinaldine ethiodide, lepidine ethiodide, or Fischer's base hydriodide.

[2 : 5-(1 : 6-*Dioxojulolidine*)][*bis*-4-(*dimethylaminobenzene*)]*dimonomethin*merocyanine (IV; X = CH).—A solution of the base (I; R = H) (1 g.) and *p*-dimethylaminobenzaldehyde (1·5 g., 2 mols.) in ethanol (25 c.c.) containing 10% aqueous sodium hydroxide (0·5 c.c.) was boiled under reflux for 15 min., an orange solid separating from the yellow solution. After cooling, the solid was collected and crystallised from dioxan, giving the mero*cyanine* (IV; X = CH), bright orange needles, m. p. 247—248° (1·2 g., 52%) (Found: C, 77·7; H, 6·4; N, 8·85. $C_{35}H_{39}O_2N_3$ requires C, 77·7; H, 6·3; N, 9·05%).

*The Dimonoazamethin*merocyanine (IV; X = N).—A solution of *p*-nitrosodimethylaniline hydrochloride (10 g., 2·2 mols.) in water (50 c.c.) at 60° was slowly added with stirring to one of the diketone (I; R = H) (5 g.) in a mixture of ethanol (50 c.c.) and 10% aqueous sodium hydroxide (50 c.c.), also at 60°, the initial reddish colour of the diketone solution rapidly becoming almost black, with separation of dark purple crystals. The latter, collected from the cold mixture and recrystallised from much acetone, afforded the mero*cyanine* (IV; X = N), blue-purple crystals, m. p. 277° (decomp.) (E.T.) (7 g., 61%) (Found: C, 72·1; H, 5·9; N, 15·2. $C_{33}H_{37}O_2N_5$ requires C, 72·2; H, 5·85; N, 15·05%).

1 : 2 : 5 : 6-*Tetra-oxojulolidine* (V or VI).—A solution of the dye (IV; R = N) (0·5 g.) in concentrated hydrochloric acid (20 c.c.) was boiled under reflux for 30 min., the initial deep red colour changing to pale yellow-brown and brown crystals separating. The crystals, being insoluble, were purified by washing with much dilute hydrochloric acid, water, and acetone, and thus afforded the *compound* (V or VI), m. p. *ca.* 440° (with sublimation) (0·15 g., 60%) (Found: C, 63·1; H, 3·4; N, 5·9. $C_{13}H_7O_4N$ requires C, 62·9; H, 3·1; N, 6·1%). Many attempts under a variety of conditions to condense this compound with *o*-phenylenediamine failed.

Action of Nitrous Acid on the Diketone (I; R = Me).—An aqueous solution of sodium nitrite in slight excess was slowly added with stirring to one of the diketone (I; R = Me) in dilute hydrochloric acid at 5°. Dilution with water then precipitated a voluminous greenish-yellow solid, which, when cautiously and rapidly recrystallised from ethanol, gave the mustard-coloured *mononitroso*-derivative [possibly (IX)], m. p. 156° (decomp.) (E.T.) (Found: C, 64·0; H, 5·3; N, 11·3. $C_{13}H_{12}O_3N_2$ requires C, 63·9; H, 5·0; N, 11·5%).

Contact with aqueous sodium hydroxide, or boiling in ethanolic solution, converted this compound into a dark brown insoluble solid, m. p. 158° (decomp.) (E.T.) (Found: C, 64·0; H, 4·8; N, 11·35%).

We are greatly indebted to Imperial Chemical Industries Limited, Dyestuffs Division, for the following report on the sensitising action of the dyes (III), (IV; X = CH), and (IV; X = N).

" The compounds were examined in solution and in a chlorobromide photographic emulsion. The properties of the solutions were :

Compound	Solvent	Concn.	Absorption max. (mμ)	Half-width (mμ)	Mol. extinction coefficient
(III)	Methanol	5×10^{-6}	523	60	$12{\cdot}2 \times 10^4$
(IV; X = CH)...	2-Ethoxyethanol	$1{\cdot}25 \times 10^{-4}$	409	44	$4{\cdot}4 \times 10^4$
(IV; X = N) ...	,,	2×10^{-4}	582	139	$1{\cdot}3 \times 10^4$

In the emulsion, (III) showed moderate sensitisation at 460—610 mμ with maximum at 545 mμ, but (IV; X = CH) and (IV; X = N) showed no sensitisation."

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 20th*, 1954.]

Cyclic Diarsines. Part II. 1 : 4-*Disubstituted Diethylenediarsines.*

By EMRYS R. H. JONES and FREDERICK G. MANN.

[Reprint Order No. 5706.]

The synthesis and properties of various 1 : 4-disubstituted diethylenediarsines are described. These compounds contain a novel heterocyclic ring, which constitutes the arsenic analogue of piperazine.

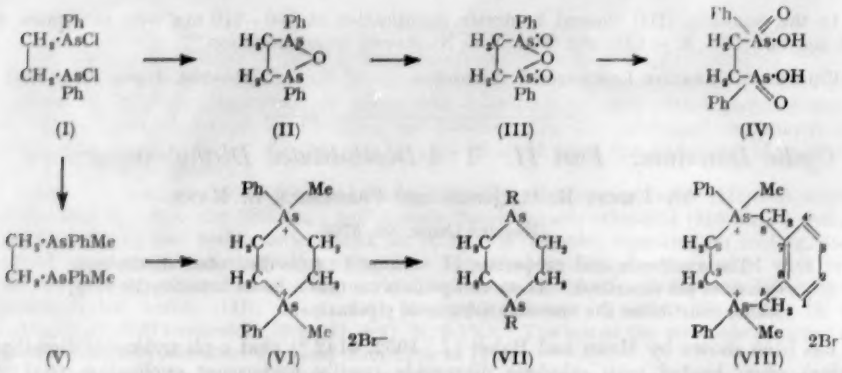
IT has been shown by Mann and Baker (*J.*, 1952, 4142 *) that *o*-phenylenebis(dimethylarsine) when heated with ethylene dibromide readily underwent cyclisation to 1 : 4-dimethylethylene-*o*-phenylenediarsine dimethobromide, and that 1 : 4-dimethylethylene-*o*-phenylenediarsine, obtained by thermal decomposition of this salt, again united with ethylene dibromide to give diethylene-*o*-phenylenediarsine dimethobromide. This type of cyclisation by double quaternisation with ethylene dibromide is clearly promoted by the tertiary arsine groups' being held rigidly in the most favourable position by the *o*-phenylene group. We have investigated a similar synthesis with the *o*-phenylene group replaced by a $\cdot CH_2 \cdot CH_2 \cdot$ group, although the great disadvantage of the conformational mobility of the arsine groups around the connecting $\cdot CH_2 \cdot CH_2 \cdot$ link was fully recognised.

Three synthetic routes have been investigated. An attempt to cyclise *s*-ethylenebis(phenylchloroarsine) (I) (Chatt and Mann, *J.*, 1939, 610) with ethylene dibromide in hot aqueous sodium hydroxide suspension, *i.e.*, by the Meyer reaction, proved abortive, because (I) readily and preferentially reacts with the alkali to form *s*-ethylenebis(phenylarsinous) anhydride, *i.e.*, 1 : 3-diphenyl-1 : 3-diarsa-2-oxa*cyclo*pentane (II), which has high stability in an alkaline medium. When treated with hydrogen peroxide, (II) gave *s*-ethylenebis(phenylarsinic) anhydride, *i.e.*, 1 : 3-diphenyl-1 : 3-diarsa-2-oxa*cyclo*pentane 1 : 3-dioxide (III), which with warm acids gave *s*-ethylenebis(phenylarsinic acid) (IV) (cf. Quick and Adams, *J. Amer. Chem. Soc.*, 1922, **44**, 805; Chatt and Mann, *loc. cit.*); consequently hot dilute nitric acid converted the cyclic (II) directly into the acid (IV). The stability of the five-membered ring in the compounds (II) and (III) recalls the ready formation of *o*-phenylenediarsine oxydichloride (Kalb, *Annalen*, 1921, **423**, 74) and the remarkably easy anhydride formation shown by compounds such as *o*-carboxyphenylmethylchloroarsine and -arsinous acid (Aeschlimann and McCleland, *J.*, 1924, **125**, 2025). Other examples of similar stable five-membered rings occur in Parts III and IV (following papers).

In a second route, diethylphenylarsine was quaternised with an excess of ethylene dibromide, but this reaction yielded a mixture of 2-bromoethyldiethylphenylarsonium bromide, $[AsEt_2Ph \cdot C_2H_4Br]Br$, and *s*-ethylenebis(diethylphenylarsonium bromide), $[AsEt_2Ph \cdot C_2H_4 \cdot AsEt_2Ph]Br_2$, both in impracticably low yields. It is highly probable that the latter product on thermal decomposition would yield ethylenebis(ethylphenylarsine), which might then undergo cyclisation with ethylene dibromide. The former compound when heated might give 2-bromoethylphenylarsine, which could then undergo a direct bimolecular cyclisation by quaternisation. Owing to the low yields, these reactions were not investigated.

* This paper is regarded as Part I of this series.

The bischloroarsine (I) was therefore converted by the Grignard reaction into ethylenebis(methylphenylarsine) (V), which however, when heated with ethylene dibromide in various proportions and at various temperatures gave only hygroscopic amorphous products, produced apparently by extensive linear condensation. Mixtures in toluene and chlorobenzene when heated gave only methylphenylarsinic acid, the foul odour



indicating that the acid probably arose by the oxidation of methylphenylarsine : this rupture of the molecule is similar to that of *s*-ethylenebis(phenylarsinic acid) which when treated with hot hydrochloric acid and sulphur dioxide gives phenyldichloroarsine (Chatt and Mann, unpublished work).

When however an equimolecular mixture of the diarsine (V) and ethylene dibromide in methanol was heated to 100°, 1 : 4-dimethyl-1 : 4-diphenyldiethylenediarsonium dibromide (1 : 4-diphenyl-1 : 4-diarsa*cyclo*hexane dimethobromide) (VI) was formed, accompanied by a considerable quantity of polymeric material. The dibromide (VI), when heated under reduced pressure, readily gave the crystalline 1 : 4-diphenyldiethylenediarsine (1 : 4-diphenyl-1 : 4-diarsa*cyclo*hexane) (VII; R = Ph). These compounds are the first examples of a novel heterocyclic system, the arsenic analogue of piperazine.

The tertiary arsine groups in (VII; R = Ph) have normal reactivity : for example, a solution of the arsine in cold methyl iodide forms a monomethiodide, and when boiled a dimethiodide; the arsine, treated with warm dilute nitric acid, is oxidised to the di(hydroxynitrate). Yet all attempts to condense the arsine with ethylene dibromide to form 1 : 4-diphenyltriethylenediarsonium dibromide gave only amorphous products; trimethylene dibromide and *o*-xylylene dibromide gave similar results. This recalls the properties of 1 : 2 : 2 : 4 : 5 : 5-hexamethylpiperazine (Mann and Senior, *J.*, 1954, 4476), which readily gives diquaternary salts with simple alkyl halides, but will not undergo diquaternisation with alkylene dibromides. The explanation may be the same for both compounds, namely, that they are " locked " in the Z form, and cannot thus assume the C form in which only could this cyclisation occur.

It is noteworthy that no indication of *cis–trans*-isomerism could be detected in the dibromide (VI) or in the corresponding di-iodide or ditoluene-*p*-sulphonate, although theoretically this isomerism could exist irrespective of the conformation of the ring system.

In order to give a possibly less rigid molecule, an attempt was made to replace the phenyl groups in the diarsine by methyl groups. Several examples are known (for references, see Mann, Millar, and Smith, *J.*, 1953, 1131) of phenyl groups, attached to cyclic arsenic atoms, being replaced by iodine by the action of hot hydriodic acid. This reagent, however, disrupted the ring in (VII; R = Ph), with the formation of *s*-ethylenebis(di-iodoarsine). Hot hydrobromic acid however gave the colourless crystalline 1 : 4-dibromodiethylenediarsine (VII; R = Br), which with methylmagnesium bromide gave the liquid 1 : 4-dimethyldiethylenediarsine (VII; R = Me).

Attempts to condense this diarsine with ethylene dibromide, by heating an equimole-

cular mixture alone at 125°, or in methanol at 100°, gave a hygroscopic amorphous product, apparently again formed by extensive linear condensation. This product moreover yielded no crystalline derivatives, and gave no decisive product on thermal decomposition. It is probable that the conditions necessary for the required cyclic condensation could be discovered, but the low over-all yield of (VII; R = Me) precluded further investigation.

A novel type of heterocyclic system was obtained by the condensation of *s*-ethylenebis(methylphenylarsine) (V) and *o*-xylylene dibromide, which yielded 1 : 4-diphenyl-1 : 4-diarsa-6 : 7-benzo*cyclo*oct-6-ene dimethobromide (VIII), together with much yellow resinous material. The salt (VIII) was deliquescent and was therefore converted by sodium iodide into the dimethiodide; thermal decomposition under reduced pressure of both these salts gave a yellow syrup which on attempted oxidation or quaternisation gave no solid derivatives.

Experimental

Unless otherwise stated, all compounds were colourless, and molecular weights were determined ebullioscopically in acetone.

s-Ethylenebis(phenylarsinous) Anhydride (II).—*s*-Ethylenebis(phenylchloroarsine) (I) (5·0 g.) and a solution of sodium hydroxide (4·0 g., 8 mols.) in water (10 c.c.) were boiled under reflux for 3 hr., and the oily product, which solidified on cooling, was recrystallised from methanol, affording the *anhydride* (II), m. p. 94° (Found: C, 48·2; H, 4·2%; *M*, 336. $C_{14}H_{14}OAs_2$ requires C, 48·3; H, 4·0%; *M*, 348). The addition of ethylene dibromide (1·1 c.c., 1 mol.) or of trimethylene dibromide (1·3 c.c., 1 mol.) to the above mixture gave the same result.

s-Ethylenebis(phenylarsinic) Anhydride (III).—Aqueous hydrogen peroxide (30%) was added dropwise to a solution of the anhydride (II) (1 g.) in acetone (15 c.c.), heat being evolved with deposition of the anhydride (III), which crystallised from ethanol as a *monohydrate*, m. p. 191° (effervescence) (Found: C, 42·5; H, 4·3. $C_{14}H_{14}O_3As_2,H_2O$ requires C, 42·2; H, 4·0%).

The anhydride (III) readily dissolved in warm dilute hydrochloric acid, which on cooling precipitated the crystalline arsinic acid (IV), m. p. 200° (effervescence) (Found: C, 42·2; H, 4·1. Calc. for $C_{14}H_{16}O_4As_2$: C, 42·2; H, 4·0%). Use of the anhydride (II) and warm dilute nitric acid in the experiment also gave (IV), m. p. and mixed m. p. 200° (effervescence).

Diethylphenylarsine and Ethylene Dibromide.—A mixture of the arsine (5·4 g.) and the dibromide (22·5 c.c., 10 mols.) was boiled under reflux in nitrogen for 6 hr., and cooled. The yellow oil which separated above the excess of dibromide was collected, and when set aside for several days became semicrystalline. These crystals were extracted with boiling acetone (10 c.c.). The insoluble residue consisted of the very hygroscopic *s*-ethylenebis(diethylphenylarsonium) dibromide, which was therefore precipitated in ethanolic solution as the *dipicrate*, yellow crystals, m. p. 166—167° (decomp.) (*ca.* 0·1 g.) (Found: C, 45·4; H, 4·2; N, 9·25. $C_{34}H_{38}O_{14}N_6As_2$ requires C, 45·2; H, 4·2; N, 9·3%).

The acetone filtrate slowly deposited *2-bromoethyldiethylphenylarsonium bromide* (*ca.* 0·1 g.), m. p. 106° after further crystallisation from acetone (Found: C, 36·2; H, 4·5. $C_{12}H_{19}Br_2As$ requires C, 36·2; H, 4·8%).

The high proportion of ethylene dibromide in the above experiment was employed to increase the yield of the second product, which appeared the more promising for subsequent cyclisation. The use of ethylene dibromide (5 mols.) gave essentially the same result.

s-Ethylenebis(methylphenylarsine) (V).—A solution of the chloroarsine (I) (50 g.) in benzene (200 c.c.) was slowly added to a cooled stirred Grignard reagent prepared from methyl iodide (31 c.c., 4 mols.) and magnesium (12·0 g., 4 atoms) in ether (200 c.c.); the mixture was then stirred for 45 min. at 15° and boiled under reflux for 30 min., all operations being performed under nitrogen. After hydrolysis with ammonium chloride (100 g.) in water (400 c.c.) the organic layer was separated, dried, and distilled under nitrogen, giving the *diarsine* (V), b. p. 163—165°/0·2 mm. (33·2 g., 74%) (Found: C, 52·7; H, 5·4. $C_{16}H_{20}As_2$ requires C, 53·0; H, 5·5%).

For characterisation, the diarsine was dissolved in cold methyl iodide, from which the *dimethiodide* was deposited, and after crystallisation from water, decomposed at *ca.* 250° without melting (Found: C, 33·6; H, 4·2. $C_{18}H_{26}I_2As_2$ requires C, 33·4; H, 4·0%). This salt furnished the *dimethopicrate*, yellow crystals, m. p. 217—218° (decomp.), from aqueous ethanol (Found: C, 42·4; H, 3·4; N, 10·1. $C_{30}H_{30}O_{14}N_6As_2$ requires C, 42·4; H, 3·5; N, 9·9%). The diarsine in acetone solution was readily converted by hygrogen peroxide into the dioxide,

which was precipitated as the *di(hydroxypicrate)*, yellow crystals, m. p. 171—172° (decomp.), from water (Found : C, 39·6; H, 3·2; N, 9·95. $C_{28}H_{26}O_{16}N_6As_2$ requires C, 39·4; H, 3·05; N, 9·85%).

1 : 4-*Dimethyl*-1 : 4-*diphenyldiethylenediarsonium Dibromide* (VI).—A solution of the diarsine (V) (23·1 g.) and ethylene dibromide (5·32 c.c., 1 mol.) in methanol (35 c.c.) was heated in a tightly stoppered bottle at 100° for 6 hr. The cold solution was diluted with ethanol (100 c.c.), and after 1 hr. the deposited crystalline *dibromide* (VI) (4·1 g.) was collected and recrystallised from methanol; it sublimed at *ca.* 255° (some decomp.) (Found : C, 39·5; H, 4·7. $C_{18}H_{24}Br_2As_2$ requires C, 39·3; H, 4·4%). The initial filtrate, when set aside for 1 day, deposited a second crop (3·4 g., 21% in all) of the dibromide. Evaporation of this filtrate then gave a sticky gum which could not be crystallised and from which well-defined derivatives could not be obtained.

The dibromide gave a *dimethopicrate*, yellow crystals, m. p. 244° (decomp.), from dimethylformamide (Found : C, 42·75; H, 3·2; N, 9·95. $C_{30}H_{28}O_{14}N_6As_2$ requires C, 42·6; H, 3·3; N, 9·9%).

A solution of the diarsine (V) (10·2 g.) and ethylene dibromide (2·44 c.c., 1 mol.) in toluene (70 c.c.) was boiled under reflux in nitrogen for 8 hr., and then concentrated under reduced pressure to *ca.* 10 c.c. and diluted with ether (80 c.c.). The white solid which slowly separated furnished methylphenylarsinic acid, m. p. and mixed m. p 175° after crystallisation from much acetone (Found : C, 42·3; H, 4·6%; *M*, ebullioscopic in ethanol, 208. Calc. for $C_7H_9O_2As$: C, 42·0; H, 4·5%; *M*, 200). Bertheim (*Ber.*, 1915, **48**, 350) gives m. p. 179·5°. The solubility of the acid in various liquids and the pH of its aqueous solution agree with those recorded by Gibson and Johnson (*J.*, 1928, 92). Use of chlorobenzene instead of toluene in the above experiment gave the same result.

1 : 4-*Diphenyldiethylenediarsine* (VII; R = Ph).—The dibromide (VI) (44 g.) was gently heated at 0·5 mm. with a brush flame until decomposition was complete. The brown distillate and the charred residue were together extracted with boiling chloroform (75 c.c.), which was then boiled (charcoal), filtered, evaporated to *ca.* 40 c.c., and diluted with hot ethanol (40 c.c.). The solution on cooling deposited the *diarsine* (VII; R = Ph), m. p. 142—144° after crystallisation from acetone (Found : C, 53·6; H, 5·2%; *M*, 346. $C_{16}H_{18}As_2$ requires C, 53·3; H, 5·0%; *M*, 360) : 8·4 g., 29%. The yield was not improved by carrying out the thermal decomposition in a Silicone bath at 300°.

A solution of this diarsine in an excess of cold methyl iodide deposited the *monomethiodide*, m. p. 211° (effervescence) after crystallisation from ethanol (Found : C, 40·3; H, 4·1. $C_{17}H_{21}IAs_2$ requires C, 40·6; H, 4·2%). The above solution, when boiled under reflux for 4 hr., gave the *dimethiodide*, m. p. 221° (effervescence) after crystallisation from methanol (Found : C, 33·6; H, 3·8. $C_{18}H_{24}I_2As_2$ requires C, 33·5; H, 3·7%). A mixture of the diarsine and methyl toluene-*p*-sulphonate (2 mols.) when heated at 150° for 1 hr. furnished the *di(methotoluene*-p-*sulphonate)*, m. p. 266° (effervescence) after crystallisation from ethanol (Found : C, 52·9; H, 5·4. $C_{32}H_{36}O_6S_2As_2$ requires C, 52·45; H, 5·2%); this salt, which has almost the same carbon and hydrogen content as the mono(methosulphonate), was identified by conversion into the above dimethiodide, m. p. and mixed m. p. 223° (effervescence).

Nitric acid, diluted with an equal volume of water, readily converted the diarsine into the *di(hydroxynitrate)*, m. p. 188° (effervescence) after crystallisation from water (Found : C, 37·5; H, 3·7; N, 5·15. $C_{16}H_{20}O_8N_2As_2$ requires C, 37·1; H, 3·8; N, 5·4%).

The diarsine, when heated with equimolecular quantities of ethylene dibromide, alone at 125° or in methanol at 100°, of trimethylene dibromide in methanol at 100°, or of *o*-xylylene dibromide in boiling toluene, gave in each case apparently amorphous products which furnished no crystalline derivatives.

A mixture of the diarsine (VII; R = Ph) (1 g.) and hydriodic acid (20 c.c.) of constant b. p., when boiled under reflux for 2 hr., gave an oil which solidified on cooling and when recrystallised from chloroform afforded s.-*ethylenebis(di-iodoarsine)*, deep yellow crystals (0·4 g., 20%), m. p. 136° (Found : C, 4·2; H, 1·0. $C_2H_4I_4As_2$ requires C, 3·5; H, 0·65%). Acetone solutions of this compound and of piperidine *N*-pentamethylenedithiocarbamate when mixed deposited s.-*ethylenebis[tetrakis-(N-pentamethylenethiocarbamoylthio)arsine]*, m. p. 198—199° (effervescence) after crystallisation from acetone (Found : C, 37·9; H, 5·0. $C_{36}H_{44}N_4S_8As_2$ requires C, 38·1; H, 5·4%).

Repetition of the above experiment using, however, hydrobromic acid (20 c.c.) of constant b. p., and boiling for 3 hr., gave an oil which also solidified on cooling, and afforded 1 : 4-*dibromodiethylenediarsine* (VII; R = Br), m. p. 168—170° after crystallisation from acetone (Found : C, 13·35; H, 2·2. $C_4H_8Br_2As_2$ requires C, 13·1; H, 2·2%). It similarly gave 1 : 4-

di-(N-*pentamethylenethiocarbamoylthio*)*diethylenediarsine* (VII; R = $C_5H_{10}N{\cdot}CS_2$·), m. p. 185—186° (effervescence) after crystallisation from chloroform (Found: N, 5·4. $C_{16}H_{28}N_2S_4As_2$ requires N, 5·3%).

1 : 4-*Dimethyldiethylenediarsine* (VII; R = Me).—A solution of the dibromodiarsine (4·2 g.) in benzene (100 c.c.) was added under nitrogen to a Grignard reagent prepared from methyl iodide (2·9 c.c., 4 mols.) and magnesium (1·10 g., 4 atoms) in ether (50 c.c.), which was then boiled under reflux for 15 min. and hydrolysed with aqueous ammonium chloride. The organic layer, when dried and distilled under nitrogen, gave the *diarsine* (VII; R = Me) (1·5 g., 56%), b. p. 113—114°/24 mm. (Found: C, 30·9; H, 6·0. $C_6H_{14}As_2$ requires C, 30·5; H, 5·9%).

When a mixture of this diarsine and ethylene dibromide (1 mol.) was heated alone at 125°, or in methanol at 100° for 3 hr., only an amorphous hygroscopic material [Found: C, 21·8; H, 5·1. Calc. for $(C_8H_{18}Br_2As_2,H_2O)_n$: C, 21·7; H, 4·6%)] was formed. This product when heated at 0·5 mm. decomposed with much blackening; the residue was extracted with warm dilute nitric acid, which was evaporated to dryness in a desiccator, giving a colourless non-crystalline residue which furnished an amorphous picrate. Lack of material prevented further investigation of the diarsine.

A mixture of the diarsine (V) (4·23 g.) and powdered *o*-xylylene dibromide (3·08 g., 1 mol.) under nitrogen rapidly set to a hard mass, which was heated at 100° for 1 hr. The crude deliquescent dimethobromide (VIII) was extracted with ethanol, leaving a yellow resinous material. The extract, added to an excess of sodium iodide in ethanol, deposited 1 : 4-*diphenyl*-1 : 4-*diarsa*-6 : 7-*benzo*cyclo*oct*-6-*ene dimethiodide diethanolate* (as VII), m. p. 160—161° (effervescence), when recrystallised from ethanol (Found: C, 41·7; H, 4·55. $C_{24}H_{32}I_2As_2,2C_2H_6O$ requires C, 41·4; H, 4·9%).

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Cyclic Diarsines. Part III. Compounds containing an Eight-membered Diarsine Ring System.*

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o-Phenylenebis(dimethylarsine) and 1 : 4-dimethylethylene-*o*-phenylenediarsine readily undergo cyclisation with *o*-xylylene dibromide and its 4-chloro-derivative to give compounds of types (IV) and (V), the stereochemistry of which is discussed. The thermal decomposition of the salts (IV) and (V) follows a novel course, with the formation of *o*-phenylenebis(2-*iso*arsindoline), or its chloro-derivative, in each case.

IT has been shown in Part I (Mann and Baker, *J.*, 1952, 4142) that *o*-phenylenebis(dimethylarsine) (I) readily combines with ethylene dibromide to give the cyclic dimethobromide (II) which on thermal decomposition gives 1 : 4-dimethylethylene-*o*-phenylenediarsine (III); the latter retains this power of cyclisation by diquaternisation, for further reaction with ethylene dibromide followed by thermal decomposition gives diethylene-*o*-phenylenediarsine. This reaction is not limited to the formation of six-membered rings, for the diarsine (I) reacts with trimethylene dibromide to form 1 : 4-dimethyltrimethylene-*o*-phenylenediarsine dimethobromide (Glauert and Mann, *J.*, 1950, 682). We have now investigated the action of *o*-xylylene dibromide, $C_6H_4(CH_2Br)_2$, on the diarsines (I) and (III), for the stereochemistry and reactions of the products are of considerable interest.

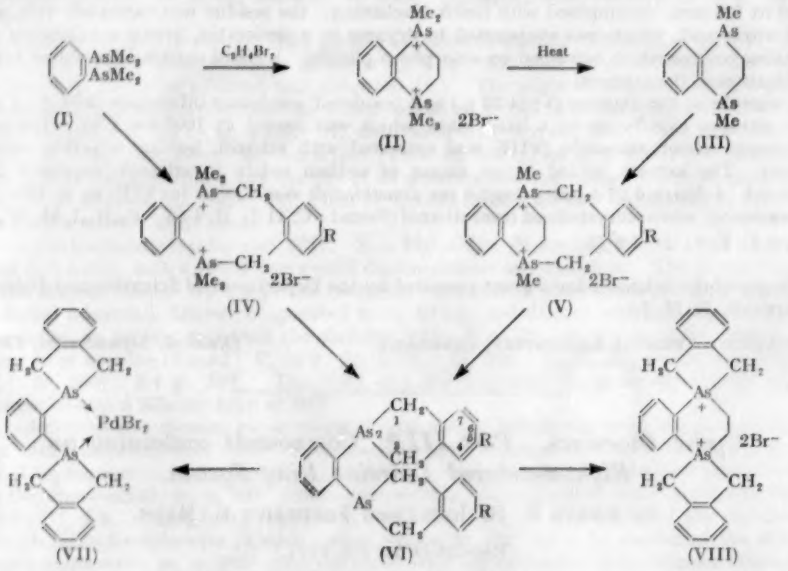
The diarsines (I) and (III) react readily and exothermally with the powdered dibromide

* Part II, preceding paper.

to form 1 : 4-dimethyl-*o*-phenylene-*o*-xylylenediarsine dimethobromide (IV; R = H) and ethylene-*o*-phenylene-*o*-xylylenediarsine dimethobromide (V; R = H) respectively. The fact that each reaction has involved cyclisation by diquaternisation is proved by the precipitation of the corresponding dimethopicrates when cold ethanolic solutions of the bromides are treated with sodium picrate. The readiness of the cyclisation is demonstrated by the rapid formation of (IV; R = H) in an equimolecular solution of (I) and *o*-xylylene dibromide in warm methanol and (more slowly) in cold benzene.

The use of 4-chloro-*o*-xylylene dibromide gave precisely similar salts (IV and V; R = Cl).

The reactions of these salts initially appeared to indicate that they were each formed by the union of two molecules of the diarsine with two of the dibromide. An *X*-ray



crystal investigation of the salt obtained by the reaction of (I) and the dibromide, kindly performed by Dr. W. Cochran in the Cavendish Laboratory of the University of Cambridge, has shown conclusively, however, that it has the "monomer" structure (IV; R = H). Moreover, crystals of (IV; R = H) and (V; R = H) are isomorphous, and the two salts have therefore essentially the same structure. A scale model of the cation of (IV; R = H) shows that the distances apart of the two arsenic atoms and of the two methylene groups are almost identical, and that the two As–CH_2 bonds are therefore almost parallel: furthermore, the tetrahedral angle at the methylene groups will cause the cyclic nucleus of the *o*-xylylene group to be tilted above or below the plane of the two As–CH_2 bonds, and geometric isomerism is therefore possible. This is shown in the schematic Figs. 1 and 2 of the *trans*- and *cis*-cations, in which hydrogen atoms have been omitted for simplicity. In each model, the benzene ring A, the arsenic atoms 1 and 4, and the methyl groups 2 and 2′ can be regarded as being in the plane of the paper, but the methyl groups 3 and 3′ are projecting towards, and the methylene groups 5 and 5′ projecting away from, the observer. In the *trans*-form (Fig. 1), the benzene ring B projects away from A: it is, however, almost parallel to A, but lies of course below the plane of the paper. In the *cis*-form (Fig. 2) the ring B is bent backward towards A, and is inclined at an angle to A, again below the plane of the paper.

Similar models of (V; R = H) can be constructed; they differ from those shown in

FIG. 1.

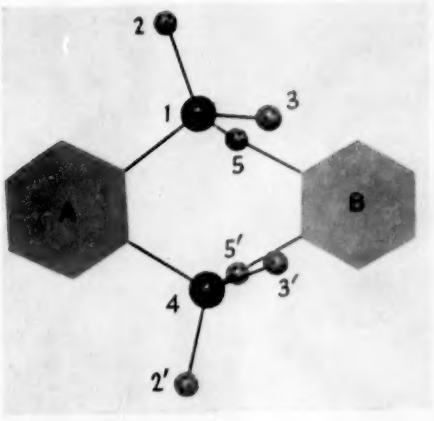
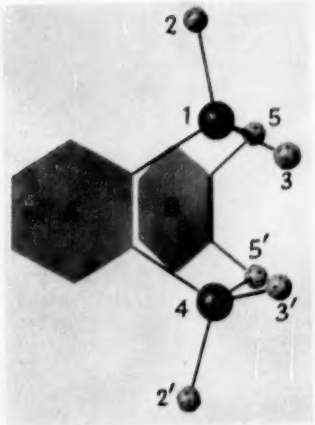


FIG. 2.



The trans- (Fig. 1) *and the* cis-*form* (Fig. 2) *of the cation of* 1 : 4-*dimethyl-o-phenylene-o-xylylene-diarsine dimethobromide* (IV; R = H).

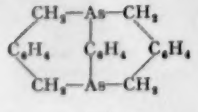
[*To face p.* 496.

Figs. 1 and 2 only in that the methyl groups 3 and 3′ now become methylene groups which, being linked, are therefore rather closer together; this constriction tends to bring the methyl groups 2 and 2′ very slightly above the plane of the paper.

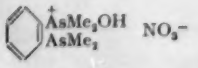
Each of the four dibromides (IV; R = H and Cl) and (V; R = H and Cl) formed homogeneous crystals, and no indication of the above isomerism could be detected. The *X*-ray investigation provides strong indication that (IV; R = H) has the *trans*-form, but a complete structure investigation has not been made. The stereochemistry of the eight-membered ring in (IV; R = H) bears some analogies to that of *s*-dibenzo*cyclo*octadiene (Baker, Banks, Lyon, and Mann, *J.*, 1945, 27), which, although theoretically capable of similar *cis*- and *trans*-isomerism, also occurred in only one form which had a centre of symmetry and hence was the *trans*-isomer.

It will be clear that each form of the compound (IV; R = Cl) and of (V; R = Cl) should be capable of optical resolution: even if *cis*- ⇌ *trans*-interconversion did occur in solution (although no mechanism for this process is apparent) it is highly improbable that the cation could pass through a symmetric phase, particularly in the case of (V; R = Cl). Fractional crystallisation of the di-(+)-camphorsulphonate and di-(+)-bromocamphorsulphonate derived from this salt gave, however, no indication of resolution, and the (+)-antimonyl tartrate, (−)-*N*-1′-phenylethylphthalamate, (+)-tartrate, and (−)-menthoxyacetate were too hygroscopic for effective recrystallisation.

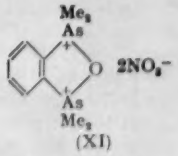
Thermal decomposition of the bromides (IV) and (V) follows an entirely novel course for quaternary arsonium halides. When the bromides (IV and V; R = H) were heated just above their m. p. at *ca.* 20 mm., steady effervescence occurred, the main product in each case being *o*-phenylenebis-(2-*iso*arsindoline) (VI; R = H). The bromides (IV and V; R = Cl) similarly gave *o*-phenylenebis-[2-(5-chloro*iso*arsindoline)] (VI; R = Cl). The identity of (VI; R = H) has been established by: (*a*) analysis and molecular-weight determinations; (*b*) chelation with palladium dibromide to form dibromo-[*o*-phenylenebis-(2-*iso*arsindoline)]palladium (VII), a reaction similar to that shown by the diarsine (I) (Chatt and Mann, *J.*, 1939, 1622); (*c*) its ready condensation with ethylene dibromide to form bis(*iso*arsindoline-*As*-*spiro*)ethylene-*o*-phenylenediarsonium dibromide (VIII), a reaction which is again precisely analogous to that of (I) ⟶ (II). These reactions show that this arsine cannot be the isomeric *o*-phenylene-di-*o*-xylylenediarsine (IX); moreover,



(IX)



(X)



(XI)

for structural reasons it is highly improbable that the ring system shown in (IX) can exist, for if the two tertiary arsenic atoms retained their normal intervalency angle (*ca.* 100°) whilst linked through an *o*-phenylene group, they could not also accommodate two " bridging " *o*-xylylene groups, since each group would require two parallel As–CH_2 bonds.

The course of the above thermal decomposition must clearly involve a rupture of the eight-membered ring in both (IV) and (V). It is possible that the first stage is dissociation of the salt to the diarsine (I or III) and *o*-xylylene dibromide, followed by condensation of two molecules of the dibromide and one of the diarsine, with elimination of methyl (and ethylene) groups, to form the diarsine (VI), the remaining diarsine unit (I or III) being discarded in some form. This possibility is supported by the fact that an equimolecular mixture of (IV; R = H) and the dibromide, when subjected to thermal decomposition under the same conditions as those of (IV; R = H) alone, gave twice the yield of the diarsine (VI). In the decomposition of the salt (IV; R = H), no free diarsine (I) could be detected. The mother-liquor from the crystallisation of the crude diarsine (VI) gave, however, a picrate which could not be identified, but which in turn gave a nitrate, the composition of which, after repeated crystallisation, indicated that it was *o*-phenylenebis(dimethylarsine) hydroxynitrate (X). Attempts to oxidise the

diarsine (I) for comparison gave, however, the anhydride (XI) of the di(hydroxynitrate), and insufficient supplies of the decomposition product were available for complete identification.

It should be noted that simple loss of methyl bromide, *i.e.*, loss without ring fission, from (IV) and (V) would give the ditertiary arsines, 1 : 4-dimethyl-*o*-phenylene-*o*-xylylenediarsine and ethylene-*o*-phenylene-*o*-xylylenediarsine respectively. Again, it is improbable that the latter compound could exist, for the two arsenic atoms, when linked through an ethylene and an *o*-phenylene group, could not accommodate an *o*-xylylene group. These considerations do not apply to the former diarsine, which has a strainless ring system. The reason for its non-formation during the thermal decomposition of (IV) is presumably that rupture of the eight-membered ring precedes loss of methyl bromide. We have, therefore, prepared *o*-phenylenebis(dibenzylarsine) in order to obtain the tetrabenzyl analogue of (IV), from which a readier loss of benzyl bromide might have been effected. The bis(dibenzylarsine) was isolated solely as a gum, which gave a crystalline monomethiodide, but only hygroscopic syrups and gums by reaction with *o*-xylylene dibromide and its 4-chloro-derivative.

Experimental

Compounds were colourless unless otherwise stated. M. p.s of the dibromides (IV) and (V) depended on the temperature of immersion, denoted as (I.T.); these salts all melted with effervescence. Molecular weights were determined in boiling benzene. The yields stated are throughout those of the once-recrystallised material.

The diarsine (I) was prepared by Chatt and Mann's method (*J.*, 1939, 610). The identity of the purified diarsine (III), b. p. 99—101°/0·5 mm., was checked by conversion into its dimethobromide, m. p. and mixed m. p. 253° (effervescence).

1 : 4-*Dimethyl*-o-*phenylene*-o-*xylylenediarsine Dimethobromide* (IV; R = H).—(*A*) A stirred mixture of the diarsine (I) (27·2 g.) and finely powdered *o*-xylylene dibromide (25·2 g., 1 mol.) rapidly became warm and within 30 min. had solidified; it was then heated at 100° for 1 hr. to ensure complete reaction, and the cold product, when recrystallised from methanol, furnished the hygroscopic *dimethobromide monohydrate*, m. p. 214—216° (I.T. 160° or 200°) (Found: C, 38·4; H, 4·9. $C_{18}H_{24}Br_2As_2,H_2O$ requires C, 38·1; H, 4·6%): 39·5 g., 75%. Treatment with sodium picrate, each in methanolic solution, yielded the *dimethopicrate*, yellow crystals (from water), m. p. 219—220° (decomp.) (Found: C, 42·45; H, 3·2; N, 10·1. $C_{30}H_{28}O_{14}N_6As_2$ requires C, 42·6; H, 3·3; N, 9·9%).

(*B*) Solutions of the diarsine (2·99 g.) and the dibromide (2·76 g., 1 mol.), each in warm methanol (30 c.c.), when mixed under nitrogen, gave within 1—2 min. a crystalline deposit (3·6 g.) of the dimethobromide, m. p. and mixed m. p. 213—215° (I.T. 160°), which gave the the dimethopicrate, m. p. 219° (decomp.), alone and mixed. Similarly, solutions of the diarsine (1·32 g.) and the dibromide (1·22 g., 1 mol.), each in benzene (100 c.c.), were mixed under nitrogen and set aside for several days; the dimethobromide (1·15 g.) slowly separated, and gave the dimethopicrate (Found: C, 42·8; H, 3·3; N, 10·3%), m. p. and mixed m. p. 218° (decomp.), after recrystallisation.

Dr. W. Cochran reports on the monohydrated dimethobromide (IV; R = H): "The crystals are orthorhombic, with unit-cell dimensions $a = 17·5$, $b = 11·3$, $c = 10·2$ Å (±2%). ($h00$) Reflections were absent for h odd, ($0k0$) for k odd, and ($00l$) for $l = 1$, 3, and 5; there were no other absences. The space group is therefore $P2_12_12_1$. The density is $1·66MZ/V$, where M is the molecular weight, Z is the number of molecules per unit cell (4 for $P2_12_12_1$), and $V = abc$. Hence density = 1·86 for the monomer (as IV; R = H), and 3·72 for the dimer. The density experimentally determined = 1·79 ± 0·1 g./c.c. and the compound is therefore the monomer.

"The crystals grow as needles with the c axis as the needle axis. The growth of a crystal in this way very rarely occurs unless the molecules are rather flat, with the plane of the molecule perpendicular to the needle axis. The *trans*-structure (Fig. 1) gives a much flatter molecule than the *cis* (Fig. 2) and is thus strongly, but not conclusively, indicated."

Ethylene-o-*phenylene*-o-*xylylenediarsine dimethobromide* (V; R = H) was prepared by method (*A*) above, from the diarsine (III) (1·91 g.) and the dibromide (1·77 g., 1·05 mol.) which rapidly solidified with heat evolution, and from methanol gave the crystalline hygroscopic

monohydrate, m. p. 214—216° (I.T. 160° and 220°) (Found: C, 38·5; H, 4·6. $C_{18}H_{22}Br_2As_2,H_2O$ requires C, 38·2; H, 4·3%): 1·71 g., 47%. It gave a *dimethopicrate*, yellow crystals (from water), m. p. 221—222° (decomp.) (Found: C, 42·8; H, 3·3; N, 9·9. $C_{30}H_{36}O_{14}N_6As_2$ requires C, 42·65; H, 3·1; N, 9·95%).

A mixture of the salts (IV; R = H) and (V; R = H) had m. p. 212—213° (I.T. 160°) with softening at 207°, and 210—213° (I.T. 200°) with softening at 208°, at the same rate of heating as for the pure salts. The infra-red spectra of the salts in a Nujol mull were almost identical (as would be expected in view of their very similar structures), but in hexachlorobutadiene the dibromide (V; R = H) showed strong sharp bands at 3·36, 2·93, 2·99, and 3·46 μ with intensities decreasing in this order, whereas the dibromide (IV; R = H) showed weak bands at 3·00, 3·37, and 2·94 μ (decreasing intensities) with only a very faint indication of a band at 3·47 μ.

4′-Chloro-1 : 4-dimethyl-o-phenylene-o-xylylenediarsine dimethobromide (IV; R = Cl) *monohydrate*, similarly prepared and recrystallised, had m. p. 241—242° (I.T. 160°), 243—244° (I.T. 220°) (Found: C, 36·2; H, 4·3. $C_{18}H_{23}ClBr_2As_2,H_2O$ requires C, 35·85; H, 4·2%), which in a vacuum over phosphoric anhydride gave the anhydrous *salt* of unchanged m. p. (Found: C, 36·9; H, 4·3. $C_{18}H_{23}ClBr_2As_2$ requires C, 37·0; H, 4·0%). It gave a *dimethopicrate*, yellow crystals, m. p. 213°, from water (Found: C, 41·1; H, 3·5; N, 9·9. $C_{30}H_{27}O_{14}N_6ClAs_2$ require C, 40·9; H, 3·1; N, 9·5%).

4′-Chloro-ethylene-o-phenylene-o-xylylenediarsine dimethobromide (V; R = Cl) *monohydrate*, m. p. 236° (I.T. 160°) and 240° (I.T. 220°) (Found: C, 35·95; H, 3·8. $C_{18}H_{21}ClBr_2As_2,H_2O$ requires C, 35·7; H, 3·8%), heated at 60°/0·1 mm. for 3 hr., gave the hygroscopic anhydrous *salt* (Found: C, 37·3; H, 4·4. $C_{18}H_{21}ClBr_2As_2$ requires C, 37·1; H, 3·6%). It gave a yellow *dimethopicrate*, m. p. 213—214° (decomp.) (Found: C, 41·2; H, 3·3; N, 9·8. $C_{30}H_{25}O_{14}N_6ClAs_2$ requires C, 41·0; H, 2·9; N, 9·6%).

The dimethobromide (V; R = Cl) also gave a *dimetho-(+)-camphorsulphonate*, m. p. 298—299° (decomp.) after 3 recrystallisations from ethanol (Found: C, 51·3; H, 5·8. $C_{38}H_{51}O_8ClS_2As_2$ requires C, 51·6; H, 5·8%). A 1·3% aqueous solution had $[M]_D^{17}$ +96°; two camphorsulphonate ions should have $[M]_D$ +100° (cf. Graham, *J.*, 1912, **101**, 746). Further recrystallisation did not change the m. p. or the rotation.

The corresponding *dimetho-(+)-bromocamphorsulphonate dihydrate* after one crystallisation from methanol–ethanol had m. p. 267—268° (decomp.), increased to 271° (decomp.) by 4 recrystallisations from ethanol (Found: C, 42·5; H, 5·3. $C_{38}H_{49}O_8ClBr_2S_2As_2,2H_2O$ requires C, 42·25; H, 5·1%). A 1·10% aqueous solution had $[M]_D^{20}$ +551°; two sulphonate ions should have $[M]_D$ +556° (cf. Pope and Read, *J.*, 1910, **97**, 2201). The dimethobromide, precipitated from aqueous solution by concentrated potassium bromide, was inactive.

A mixture of the salts (IV; R = Cl) and (V; R = Cl) had m. p. 241—242° (I.T. 200° or 220°). The infra-red spectra of these salts in Nujol mull were also closely similar, but that of the former had a well-defined sharp band at 9·84 μ which was absent in that of the latter. In hexachlorobutadiene, the salt (IV; R = Cl) showed very weak rather broad bands at 2·9, 3·1, 3·38, 3·47, and 3·57 μ, whereas the salt (V; R = Cl) showed much stronger and sharper bands at 2·87 and 3·36 μ and rather weaker bands at 3·46 and 3·55 μ, but none at 3·1 μ.

Thermal Decomposition.—The dimethobromide (IV; R = H). (*A*) The pure powdered salt (3·88 g.), when cautiously heated with a small "brush" flame, melted and then gave a steady effervescence; when this ceased, the clear residual liquid readily solidified on cooling. Recrystallisation from ethanolic chloroform gave *o-phenylenebis-(2-isoarsindoline)* (VI; R = H), m. p. 129—131° (0·80 g., 53%) (Found: C, 61·0; H, 4·7%; *M*, 416. $C_{22}H_{20}As_2$ requires C, 60·9; H, 4·6%; *M*, 434).

(*B*) To ensure the mildest possible conditions for the decomposition, the powdered salt (2 g.) was heated at 0·5 mm. in a large flask (to ensure that most of the salt was in contact with the wall) immersed in a Silicone bath, the temperature being slowly increased until effervescence started and then kept constant (240—245°), the complete decomposition taking 45 min. The product, once recrystallised, gave the same product (VI; R = H), m. p. and mixed m. p. 123—129° (0·25 g., 32%).

(*C*) A powdered mixture of the salt (IV; R = H) (2·0 g.) and *o*-xylylene dibromide (0·93 g., 1 mol.), treated as in (*A*), gave the same product (0·48 g., 61%).

Evaporation of the mother-liquors from the recrystallisation of (VI; R = H) in (*A*) gave a gum, which could not be obtained solid but, treated in ethanol with sodium picrate, gum deposited a bromine-free picrate. The latter, repeatedly recrystallised from methanol, ethanol, acetone, or water, gave in each case yellow crystals, m. p. 181—182° (Found: C,

45·5, 45·65; H, 4·0, 4·05; N, 6·7, 7·1%). Since this product appeared to be mixed crystals of more than one compound, a portion (0·5 g.) was decomposed with cold dilute nitric acid and the mixture then repeatedly extracted with ether. The aqueous solution was evaporated to dryness in a desiccator at room temperature, and the residue, after repeated recrystallisation from ethanol, gave apparently *o-phenylenebis(dimethylarsine) hydroxynitrate dihydrate* (X), m. p. 196—197° (effervescence) (Found: C, 29·65; H, 4·6; N, 3·6. $C_{10}H_{17}O_4NAs_2,2H_2O$ requires C, 29·9; H, 5·2; N, 3·5%).

The dimethobromide (V; R = H). This was performed as in (*A*) above, and furnished the diarsine (VI; R = H), m. p. and mixed m. p. 129—131°, after crystallisation (Found: C, 60·9; H, 4·9%).

The dimethobromide (IV; R = Cl). This was carried out essentially as in (*A*) above, and gave *o-phenylenebis*-[2-(*5-chloroisoarsindoline*)] (VI; R = Cl), m. p. 191—195°, after crystallisation from chloroform (Found: C, 52·8; H, 3·9%; *M*, 525. $C_{22}H_{16}Cl_2As_2$ requires C, 52·5; H, 3·6%; *M*, 503).

The dimethobromide (V; R = Cl). This also gave the diarsine (VI; R = Cl), m. p. and mixed m. p. 190—195°.

Reactions of the Diarsine (VI; R = H).—A solution of the diarsine in excess of methyl iodide, when boiled for 2 hr., gave the *monomethiodide*, m. p. 180—181° (effervescence) after recrystallisation from aqueous ethanol (Found: C, 47·6; H, 4·2. $C_{23}H_{23}IAs_2$ requires C, 47·9; H, 4·0%). When a solution of the arsine (VI; R = H) in methanolic methyl iodide was heated in a sealed tube at 100° for 6 hr., it also afforded this salt, m. p. as above, alone and mixed (Found: C, 47·7; H, 4·05%). It may be noted that under these conditions the diarsine (I) gives the mono- and di-methiodide respectively (Mann and Baker, *loc. cit.*).

When a concentrated aqueous solution of potassium palladobromide was added dropwise to a boiling solution of the diarsine (VI; R = H) in acetone, *dibromo*-[*o-phenylenebis*-(2-iso-*arsindoline*)]*palladium* (VII) was deposited; it formed yellow crystals, m. p. 336—337° (decomp.), from dimethylformamide (Found: C, 37·6; H, 3·1. $C_{22}H_{20}Br_2As_2Pd$ requires C, 37·7; H, 2·85%).

A mixture of the diarsine (VI; R = H) (1·44 g.) and ethylene dibromide (0·29 c.c., 1 mol.), when heated at 125—130° for 6 hr., slowly solidified, and when then recrystallised from ethanol furnished *bis*(iso*arsindoline*-As-spiro)*ethylene-o-phenylenediarsonium dibromide monohydrate* (VIII), m. p. 223° (effervescence) (Found: C, 45·0; H, 4·1. $C_{24}H_{24}Br_2As_2,H_2O$ requires C, 45·0; H, 4·1%). It gave a *dipicrate*, yellow crystals, m. p. 216—217° (decomp., preliminary softening), from ethanolic acetone (Found: C, 47·3; H, 3·5; N, 8·9. $C_{36}H_{28}O_{14}N_6As_2$ requires C, 47·1; H, 3·1; N, 9·2%).

Oxidation of the Diarsine (I).—Samples of this diarsine were treated with cold concentrated nitric acid, warm dilute nitric acid (1 : 1 by vol.), and with hydrogen peroxide in acetone, followed later by a small quantity of dilute nitric acid. Each solution was evaporated to dryness in a vacuum-desiccator at room temperature, and the residue, when crystallised from ethanol, yielded the *anhydride* (XI), m. p. 213° (effervescence), of *o*-phenylenebis(dimethylarsine) di(hydroxynitrate) (Found: C, 28·1; H, 3·9; N, 6·5. $C_{10}H_{16}O_7N_2As_2$ requires C, 28·2; H, 3·8; N, 6·6%). It gave a *di(hydroxypicrate)* (as XI), yellow needles, m. p. 138—140°, after crystallisation from water and drying at 70°/0·1 mm. (Found: C, 34·9; H, 3·05; N, 11·0. $C_{22}H_{20}O_{15}N_6As_2$ requires C, 34·8; H, 2·7; N, 11·1%).

Addition of bromine (1 mol.) to the diarsine (I) in ethanol, followed by hydrolysis with aqueous sodium hydroxide, did not furnish an arsine oxide, and the aqueous solution did not give a picrate. Many other attempts to prepare the salt (X) by the oxidation of (I) failed.

We are greatly indebted to Dr. W. Cochran for the *X*-ray crystal investigation, and to the Department of Scientific and Industrial Research for a grant (E. R. H. J.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, September 6th,* 1954.]

Cyclic Diarsines. Part IV. Derivatives of 5 : 10-Dihydro-5 : 10-dimethylarsanthren.*

By Emrys R. H. Jones and Frederick G. Mann.

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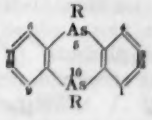
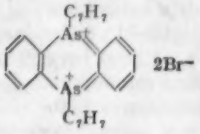
The reaction of the above arsanthren (I; R = Me) with bromine, alkyl halides, ethylene, trimethylene, and *o*-xylylene dibromides, and the formation of novel polycyclic diarsine systems, are discussed. Considerable evidence is adduced for the structure of benzenoid-quinonoid diarsonium salts of type (IV).

5 : 10-Dichloro-5 : 10-dihydroarsanthren (I; R = Cl) was first prepared by Kalb (*Annalen*, 1921, **423**, 39), and the great stability of this ring system was demonstrated by Wieland and Rheinheimer (*ibid.*, p. 10) who showed, for example, that it resisted attempts at nuclear nitration. Chatt and Mann (*J.*, 1940, 1184) prepared the 5 : 10-di-*p*-tolyl derivative (I; R = C_6H_4Me), which they isolated as two geometric isomers : this isomerism arises from the fact that the tervalent arsenic atom has an intervalency angle of *ca.* 100°, and the molecule is therefore folded about the As–As axis. This di-*p*-tolyl derivative formed a highly stable colourless dibromide, which possessed many properties of a salt, and Chatt and Mann suggested that it had the benzenoid-quinonoid structure (II).



(I)



(II)

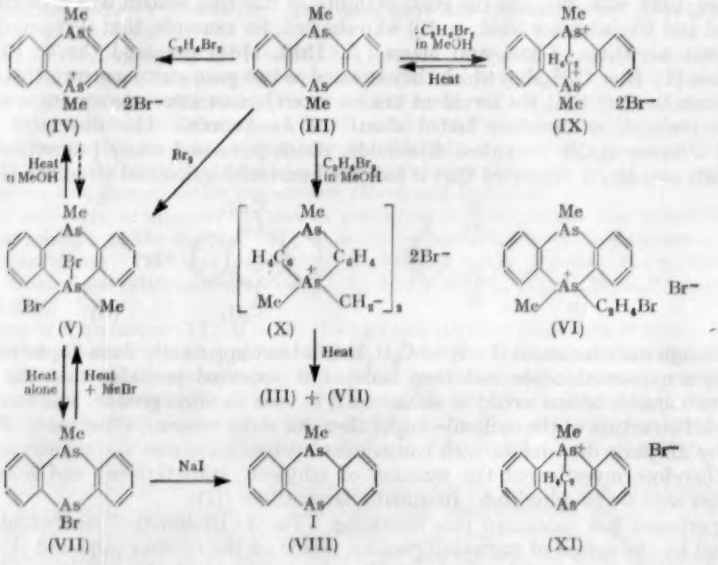
Although the compound (I; R = C_6H_4Me) did not apparently form diquaternary salts, for only a monomethiodide had been isolated, it appeared probable that the reactivity of the two arsenic atoms would be enhanced if R were an alkyl group; and moreover that the folded structure of the molecule might then, for steric reasons, allow ready diquaternisation by alkylene dibromides with consequent cyclisation across the arsenic atoms. We have therefore investigated the reaction of ethylene, trimethylene, and *o*-xylylene dibromides with 5 : 10-dihydro-5 : 10-dimethylarsanthren (III).

Experiment has confirmed this reasoning. The 5 : 10-dimethyl compound (III) was prepared by the action of methylmagnesium iodide on the chloro-compound (I; R = Cl); no attempt was made to investigate whether this product was also a mixture of geometric isomers, as such isomers would probably undergo reasonably ready interconversion at the temperatures employed in our subsequent reactions. The expected greater reactivity of the arsenic atoms was confirmed, for a solution of (III) in methanolic methyl bromide when heated at 50° for 2 hours gave the monomethobromide, but at 100° for 6 hours furnished the dimethobromide; further, the compound (III) in boiling methyl iodide gave only the monomethiodide, but with methyl toluene-*p*-sulphonate at 180° for 4 hours gave the dimethotoluene-*p*-sulphonate, which was readily converted into the dimethiodide. The stability of the ring system was again demonstrated, in that the compound (III) with a mixture of concentrated sulphuric and fuming nitric acids at 100° for 2 hours gave solely the diarsine di(hydroxynitrate), whose composition was shown by its conversion into the corresponding di(hydroxypicrate).

The interaction of the dihydrodimethylarsanthren (III) with ethylene dibromide depended markedly on the conditions employed, and gave some unexpected products. When equimolecular quantities of (III) and of the dibromide were heated at 125° for 6 hours, or at 100° for 24 hours, the only product isolated (in 60% yield after recrystallisation) was arsanthren dimethobromide (IV), identical in general structure with the compound (II). The allocation of structure (IV) is based on the following evidence. (*a*) The product

* Part III, preceding paper.

forms stable cream-coloured crystals, m. p. 256°, in which all the bromine is ionic. The bromine can therefore be estimated volumetrically in cold aqueous solution and the dibromide can be readily converted in cold methanolic solution into its di-iodide and di-picrate. (*b*) The compound (III), when heated with an equivalent of bromine in methanol at 100°, again gives the dibromide (IV). It is probable that the first action of the bromine is direct addition to one arsenic atom to give the tertiary arsine dibromide (V) which then undergoes rearrangement to the salt (IV). The mechanism by which ethylene dibromide converts (III) into (IV) is unknown. It is probable, however, that the first action is quaternisation at one arsenic atom to give (VI): the positive pole on this arsenic atom partly deactivates the second arsenic atom, and in the absence of strongly quaternising conditions (discussed below) the salt (VI) decomposes with loss of ethylene and the formation of (IV).



It is noteworthy that although the dibromide (IV) is colourless, the corresponding di-iodide, obtained from (IV) by double decomposition in solution, forms deep orange crystals; these in turn give pale yellow methanolic and ethanolic solutions, which on treatment with sodium picrate deposit the dipicrate. This indicates that the di-iodide in these solutions may exist as an equilibrium mixture of the ionic and the covalent form [as (IV) and (V) respectively], and that in the crystalline state it assumes solely the covalent form, for tertiary arsine di-iodides are normally orange to brown.

The structure of the cation in (IV) is of great interest, because it will clearly exist as a resonance hybrid closely akin in structure to anthracene; it should then have considerable stability, and in particular the whole cation, including the methyl groups, should be uniplanar. This planar factor is of importance in the structure of the *o*-xylylene derivatives (see below).

The dibromide (IV) when heated at 0·1 mm. readily lost methyl bromide with the formation of the pale yellow 5-bromo-5 : 10-dihydro-10-methylarsanthren (VII), which with sodium iodide in boiling acetone gave the 5-iodo-analogue (VIII), whose deep yellow colour is characteristic of compounds of type R_2AsI. This formation of the 5-bromo-derivative (VII) again almost certainly proceeds by way of the isomeric dibromide (V). Further, this series of reactions can be reversed, for the bromo-derivative (VII) when heated with methyl bromide at 100° is reconverted into the dibromide (IV). This might

appear to be an abnormal reaction, for the methyl bromide might be expected to quaternise the 10-methylarsine group rather than to attack the 5-bromoarsine group in (VII). It is possible that this quaternisation does occur and the product then forms the usual dissociation equilibrium; if, however, addition of methyl bromide to the 5-bromoarsine group occurs as a competing reaction, and the dibromo-derivative (V) so formed readily isomerises to the more stable dibromide (IV), the latter will ultimately be the sole product.

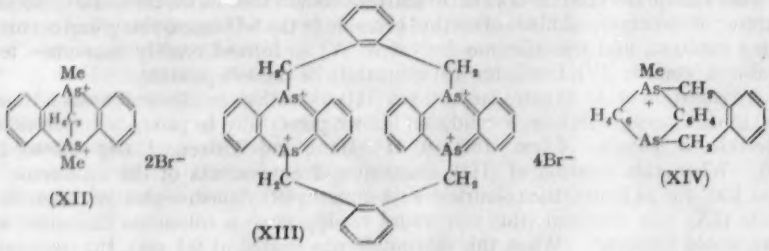
Diquaternisation of the dimethylarsanthren (III) with ethylene dibromide was ultimately achieved in methanolic solution, a condition known powerfully to promote quaternisation (Menschutkin, *Z. physikal. Chem.*, 1890, **6**, 41; Mann and Watson, *J. Org. Chem.*, 1948, **13**, 509). When this solution of (III), containing 2 equivalents of the dibromide, was heated at 100° for 24 hours, the colourless 1 : 4-dimethylethylenedi-*o*-phenylenediarsonium dibromide (IX) was obtained (this compound readily gave a colourless di-iodide, as its structure would indicate). When this dibromide was heated at 0·1 mm. the reaction was reversed, since the dimethylarsanthren (III) was again obtained. All attempts, by modifying the conditions of the thermal decomposition, to induce the alternative loss of methyl bromide and formation of ethylenedi-*o*-phenylenediarsine failed. It must be emphasised that an ethylene group bridging the two arsenic atoms, as in (IX), would apparently entail some strain in the ring system, and there is at present no decisive evidence to show whether the salt has the structure (IX) or is a " dimer " in which two ethylene groups span two arsanthren units, analogous to (XX) (p. 415). No reliable method of molecular-weight determination for such salts is available.

When, however, the methanolic solution of (III) was heated with 1 equivalent of ethylene dibromide, the main product was *s*-ethylenebis-5-(5 : 10-dihydro-5 : 10-dimethylarsanthronium) dibromide (X), which is similar in general type to *s*-ethylenebis(hexahydro-1 : 4-diphenylazarsonium) dibromide and its azaphosphonium analogue (Beeby and Mann, *J.*, 1951, 886; Mann and Millar, *J.*, 1952, 3039). The compound (X) is almost identical in composition with 1-methylethylenedi-*o*-phenylenediarsine monobromide (XI), but its identity is established by decomposition at 250°/0·1 mm. to an equimolecular mixture of the dimethyl- and bromomethyl-arsanthren (III) and (VII); there is no obvious route whereby both these compounds could arise from (XI), whereas fission of (X) could obviously produce them.

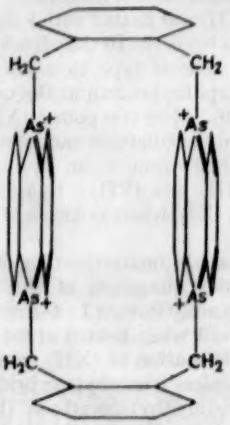
The complexities shown by ethylene dibromide quaternisation do not appear when trimethylene dibromide is used. Equimolecular quantities of the dimethylarsanthren (III) and trimethylene dibromide at 155—160° readily formed 1 : 4-dimethyltrimethylenedi-*o*-phenylenediarsonium dibromide (XII); this salt when heated at 0·1 mm. also smoothly regenerated the arsanthren (III). The ready formation of (XII), compared with that of (IX), is probably due largely to the almost strainless trimethylene bridge.

When equimolecular quantities of dihydrodimethylarsanthren (III) and *o*-xylylene dibromide were heated, two compounds were formed in proportions determined by the temperature. One is 5 : 5′-10 : 10′-bis-*o*-xylylenebisarsanthronium tetrabromide (XIII), a compound analogous to (IV) in the resonance arsanthren structure, its existence as cream-coloured crystals, and in its ready conversion into an orange tetraiodide. If each arsanthronium unit is planar, the As–CH_2 bonds must also be in this plane and must form a direct extension of the As–As axis; if so, the molecule must have the " dimer " structure (XIII), since under these conditions one *o*-xylylene radical could not span the two arsenic atoms of one arsanthren unit. The cation of (XIII) can therefore be shown as (XIIIA), in which the two planar arsanthren ring systems are depicted at right angles to the plane of the paper: for simplicity, the double bonds are shown in the quinonoid but not in the benzenoid rings. The four As–CH_2 groups are in this plane, but models show that in each *o*-xylylenediarsine unit the parallel orientation of the As–CH_2 groups causes the benzene ring of the *o*-xylylene bridge to be markedly tilted towards or away from the observer. This tilt could cause *cis–trans* isomerism: since our products were homogeneous, they probably had the symmetrical (and presumably more stable) *trans*-form. Calculations based on the data provided by Lonsdale (*Proc. Roy. Soc.*, 1929, *A*, **123**, 494; *Trans. Faraday Soc.*, 1929, **25**, 352) and Pauling (" Nature of the Chemical Bond," Cornell University Press, 2nd Edn., 1945, pp. 160 *et seq.*) indicate that the two parallel arsanthren units in

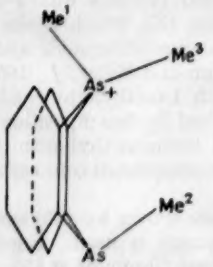
(XIIIA) would be 2·9 Å apart. In view of the shape and considerable size of this cation, it may be significant that the tetrapicrate crystallises as a decahydrate.



The second product is a colourless salt of empirical formula $(C_{21}H_{19}As_2)Br$, which can readily be converted into a colourless iodide. Several structures (p. 418) could be allocated to this compound, but an *X*-ray crystal investigation, kindly carried out in the Cavendish Laboratory of the University of Cambridge by Dr. W. Schaffer of the University of Cape Town, shows conclusively that it is di-*o*-phenylene-*o*-xylylenediarsine monomethobromide (XIV). This structure is of great interest. A model shows that if the *o*-xylylene group is thus to span the arsenic atoms, the two $As–CH_2$ bonds must be almost parallel (as in the



(XIIIA)



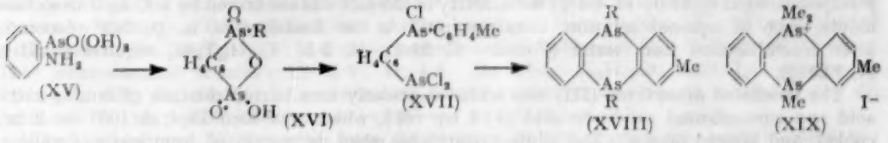
(XV)

analogous case of the *o*-xylylene derivatives of *o*-phenylenebis(dimethylarsine) and 1 : 4-dimethylethylene-*o*-phenylenediarsine: Part III). But in the dimethylarsanthren (III) and, for example, its dimethobromide, the C–As–C valency angle, of *ca.* 100° and 109° respectively in these compounds, does not allow any conformation in which the As–Me bonds of the two arsenic atoms are parallel (cf. Chatt and Mann, *loc. cit.*; Mann, *J.*, 1945, 67). In dimethylarsanthren monomethobromide [shown diagramatically as cation in (XV), where Me^1 and Me^2 represent the original methyl groups and Me^3 that inserted by quaternisation], the valency angles at the top and the bottom arsenic atom are now *ca.* 109° and *ca.* 100° respectively, so that, even allowing for some averaging of these angles in the ring system, there is one conformation, as shown, in which these As–Me bonds are almost parallel. Consequently it follows that the tricyclic diarsine structure of (XIV) can exist without marked strain only as a monoquaternary salt, in which the two $As–CH_2$ bonds have the spatial arrangement of the $As–Me^3$ and $As–Me^2$ bonds in (XV).

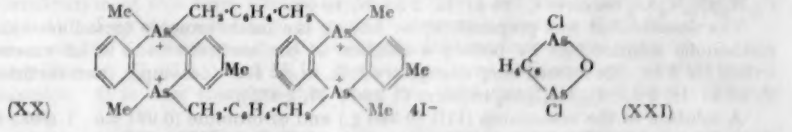
This structure is in line with the fact that the bromide (XIV) when heated in a vacuum underwent general decomposition, and no definite product could be isolated; for simple loss of methyl bromide—normally so characteristic of tertiary arsine methobromides—could not occur from (XIV).

It is noteworthy that when equimolecular quantities of the dimethylarsanthren (III) and *o*-xylylene dibromide were heated together for 2 hours at 130°, the yields of the tetrabromide (XIII) and the monobromide (XIV) were 8% and 65% respectively, and at 160° were 39% and 20%. When two equivalents of the dibromide were used, with heating for 2 hours at 160°, only the tetrabromide (XIII) was isolated; finally, the compound (XIV), when heated with one equivalent of the dibromide for 2 hours at 140—145°, gave (XIII). It is clear therefore that a reasonably ready conversion (XIV) ⟶ (XIII) must occur under these conditions: this is not surprising, in view of the great thermal lability shown by " bridged " *o*-xylylene groups in the diarsine derivatives discussed in Part III.

In view of the comparatively ready formation of the bridged salt (IX), we attempted to prepare an analogous compound having one nuclear substituent and consequently possessing molecular dissymmetry. Diazotised *o*-arsanilic acid (XV) was treated with *p*-tolylarsenoxide, C_7H_7AsO, by the Bart reaction, which afforded the anhydride (XVI; R = C_6H_4Me) of *o*-arsonophenyl-*p*-tolylarsinic acid; reduction with sulphur dioxide and hydrochloric acid then yielded chloro-(*o*-dichloroarsinophenyl)-*p*-tolylarsine (XVII), a thick oil which with hydrogen peroxide in acetone exothermally regenerated the anhydride (XVI). The chloride (XVII) underwent cyclisation when heated, to give 5 : 10-dichloro-5 : 10-dihydro-2-methylarsanthren (XVIII; R = Cl), a yellow oil, converted by methylmagnesium bromide into 5 : 10-dihydro-2 : 5 : 10-trimethylarsanthren (XVIII; R = Me), which formed a gum. With cold methyl iodide and bromide this gave the monomethiodide [probably (XIX)] and the dimethobromide respectively, both crystalline, this result recalling the work of Mole and Turner (*J.*, 1939, 1720) on the comparative activating effect on chloroarsines of nuclear methyl groups in the formation of phenoxarsines.



The trimethylarsanthren (XVIII; R = Me) reacted readily at 100° also with ethylene and trimethylene dibromide, but in each case the product, and the corresponding di-iodide, did not crystallise. The arsanthren also reacted with *o*-xylylene dibromide to give a very hygroscopic bromide, which in turn gave a non-hygroscopic crystalline iodide. The molecular complexity of this salt is uncertain, but the valency distributions about the arsonium atoms [cf. (XIV)] indicate that it is very probably the dimer, *i.e.*, 5 : 10 : 5′ : 10′-tetrahydro-2 : 5 : 10 : 2′ : 5′ : 10′-hexamethyl-5 : 5′-10 : 10′-bis-*o*-xylylenebisarsanthronium tetraiodide (XX). The monomer, in which one *o*-xylylene group bridged the arsenic atoms of one arsanthren unit, would be dissymmetric, but the dimer could exist in several geometrically isomeric forms, at least one of which has a plane of symmetry. The (+)-bromocamphorsulphonate and the antimonyl (+)-tartrate gave no indication of resolution, and other salts with optically active acid radicals were impracticably hygroscopic.



The use of *p*-methoxyphenylarsenoxide in the above Bart reaction gave the anhydride acid (XVI; R = C_6H_4·OMe), which, however, on treatment with sulphur dioxide and hydrochloric acid gave the anhydride (XXI) of *o*-phenylenebis(chlorohydroxyarsine) (cf. Kalb, *loc. cit.*; Chatt and Mann, *loc. cit.*). The use of *p*-nitrophenylarsenoxide gave an azobenzenediarsonic acid, and attempts to synthesise a suitable analogue of (IX) were discontinued.

Compounds of types (XVI) and (XXI) further illustrate the ready formation of five-membered rings containing arsenic atoms (cf. Parts II and III, preceding papers).

Experimental

Unless otherwise stated, all compounds prepared were colourless. The yields stated are those of the once-recrystallised products.

5 : 10-Dihydro-5 : 10-dimethylarsanthren (III).—A fine suspension of the dichloro-compound (I; R = Cl) (20 g.) in benzene (150 c.c.) was slowly added to a Grignard reagent prepared from methyl iodide (13·2 c.c., 4 mols.) and magnesium (4·8 g., 4 atoms) in ether (100 c.c.). The mixture was boiled under reflux for 1 hr., cooled in ice-water, and hydrolysed with ammonium chloride solution. The organic layer, when separated, dried (Na_2SO_4), and evaporated, gave a residue which when crystallised from ethanol–chloroform afforded the *arsanthren* (III) (16 g., 90%), m. p. 191—192·5° (Found: C, 50·7; H, 4·5. $C_{14}H_{14}As_2$ requires C, 50·6; H, 4·2%).

The *monomethobromide*, prepared by use of an excess of methyl bromide in methanol in a sealed tube at 50° for 2 hr., had m. p. 219° (effervescence) after crystallisation from methanol (Found: C, 42·3; H, 4·1. $C_{15}H_{17}BrAs_2$ requires C, 42·15; H, 4·0%). The *dimethobromide*, prepared similarly at 100° (6 hr.), had m. p. 302° (effervescence) after crystallisation from water (Found: C, 36·65; H, 4·1. $C_{16}H_{20}Br_2As_2$ requires C, 36·8; H, 3·8%). Its aqueous solution, treated with aqueous sodium picrate, deposited the *dimethopicrate*, yellow crystals, m. p. 282° (decomp.) after crystallisation from dimethylformamide (Found: C, 41·3; H, 3·2; N, 10·55. $C_{28}H_{24}O_{14}N_6As_2$ requires C, 41·05; H, 2·9; N, 10·3%). The *monomethiodide*, prepared by boiling a solution of (III) in methyl iodide for 1 hr., had m. p. 222° (effervescence) after crystallisation from ethanol (Found: C, 38·1; H, 3·6. $C_{15}H_{17}IAs_2$ requires C, 38·0; H, 3·6%). The *dimethotoluene-p-sulphonate*, prepared by use of methyl toluene-*p*-sulphonate (2 mols.) at 180° for 4 hr., had m. p. 316° (decomp.) after crystallisation from methanol (Found: C, 51·4; H, 4·8. $C_{30}H_{34}O_6S_2As_2$ requires C, 51·15; H, 4·8%). Since, however, the monomethotoluene-*p*-sulphonate has C, 51·0; H, 4·6%, the identity of the salt was confirmed by adding it to sodium iodide, each in aqueous solution, thus precipitating the *dimethiodide*, m. p. 263° (decomp.) after crystallisation from water (Found: C, 31·2; H, 3·0. $C_{16}H_{20}I_2As_2$ requires C, 31·1; H, 3·25%).

The powdered arsanthren (III) was added cautiously to a stirred mixture of fuming nitric acid and concentrated sulphuric acid (1 : 1 by vol.), which was then kept at 100° for 2 hr., cooled, and poured on ice. The white precipitate, when recrystallised from water, furnished the *di(hydroxynitrate)*, pale yellow crystals, m. p. 224° (effervescence) with immediate resolidification and remelting at 373° (decomp.) (Found: C, 33·9; H, 3·1; N, 5·4. $C_{14}H_{14}O_2As_2,2HNO_3$ requires C, 34·3; H, 3·3; N, 5·7%). The *di(hydroxypicrate)* formed yellow crystals, m. p. 210° (decomp.) from water (Found: C, 37·9; H, 2·7; N, 10·2. $C_{14}H_{14}O_2As_2,2C_6H_3O_7N_3$ requires C, 37·9; H, 2·4; N, 10·2%).

Reaction of the Arsanthren (III) *with Ethylene Dibromide.*—(*A*) The arsanthren (1·541 g.) and the dibromide (0·432 c.c., 1 mol.) were heated in a sealed tube at 125—130° for 6 hr. The tube, although cooled to 0° before being opened, still contained gas (probably ethylene). The cold stone-hard residue, when recrystallised from methanol, gave the cream-coloured *arsanthren dimethobromide* (IV) (1·49 g., 60%), m. p. 256° (effervescence) (Found: C, 34·1; H, 3·0; total Br, 32·4; ionic Br, 32·6; As, 30·8. $C_{14}H_{14}Br_2As_2$ requires C, 34·1; H, 2·9; Br, 32·5; As, 30·5%). From methanolic solution it readily deposited the yellow *dimethopicrate*, m. p. 244° (decomp.) after crystallisation from ethanol (Found: C, 39·35; H, 2·5; N, 10·25. $C_{28}H_{18}O_{14}N_6As_2$ requires C, 39·5; H, 2·5; N, 10·6%).

The *dimethiodide* was prepared (*a*) by adding the methobromide to sodium iodide, each in methanolic solution, (*b*) by boiling a solution of the methobromide in an excess of methyl iodide for 2 hr. It formed deep orange crystals, m. p. 214° (decomp.), from methanol (Found: C, 28·9; H, 2·2. $C_{14}H_{14}I_2As_2$ requires C, 28·7; H, 2·4%).

A solution of the arsanthren (III) (0·395 g.) and of bromine (0·061 c.c., 1 mol.) in methanol (1 c.c.) when heated at 100° for 6 hr., gave the dimethobromide (IV), m. p. and mixed m. p. 256° (effervescence), after crystallisation from methanol; this in turn gave the above dimethopicrate, m. p. and mixed m. p. 243—244° (decomp.).

When the pure dimethobromide (0·52 g.) was heated gently with a "brush" flame at 0·1 mm., effervescence occurred smoothly and the residual pale yellow liquid solidified on cooling. Recrystallisation from benzene afforded *5-bromo-5 : 10-dihydro-10-methylarsanthren* (VII) (0·34 g., 81%), pale yellow crystals, m. p. 175—177° (Found: C, 39·15; H, 2·7%; *M*, cryoscopic in benzene, 414. $C_{13}H_{11}BrAs_2$ requires C, 39·3; H, 2·75%; *M*, 397). An acetone–ethanol solution of (VII) and of sodium iodide, when boiled for 5 min. and cooled, deposited the *5-iodo-*

derivative (VIII), deep yellow crystals, m. p. 174—178°, from acetone (Found: C, 34·7; H, 2·8. $C_{13}H_{11}IAs_2$ requires C, 35·1; H, 2·5%).

When a solution of the bromo-compound (VII) in an excess of methyl bromide was heated in a sealed tube at 100° for 2 hr., it afforded the dimethobromide (IV), m. p. and mixed m. p. 256° (effervescence) after crystallisation from methanol (Found: C, 33·9; H, 3·1%). Repetition of this experiment, with methyl iodide and 1 hour's heating, afforded the dimethiodide (as IV), deep orange crystals, m. p. 214° (decomp.) alone and mixed, after crystallisation from methanol (Found: C, 28·9; H, 2·3%).

(*B*) A solution of the arsanthren (III) (1·36 g.) in ethylene dibromide (0·71 c.c., 2 mols.) and methanol (1·5 c.c.) in a sealed tube at 100° (24 hr.) afforded 1 : 4-*dimethylethylenedi-o-phenylenediarsonium dibromide monohydrate* (IX), m. p. 272° (effervescence) (from methanol) (1·2 g., 63%) (Found: C, 35·9; H, 3·7; Br, 30·0. $C_{16}H_{18}Br_2As_2,H_2O$ requires C, 35·7; H, 3·75; Br, 29·7%). Concentration of the mother-liquor ultimately yielded a trace of the dimethobromide (IV), m. p. 256° (effervescence), alone and mixed.

A methanolic solution of the dibromide (IX) readily gave the *dipicrate*, which separated from ethanol–dimethylformamide as yellow crystals, m. p. 273° (decomp.), having dimethylformamide of crystallisation (Found: C, 41·85; H, 3·0; N, 11·0. $C_{28}H_{22}O_{14}N_6As_2,C_3H_7ON$ requires C, 41·8; H, 3·3; N, 11·0%).

The dibromide (IX), when added to an excess of sodium iodide, each in methanol, deposited the *di-iodide* (as IX), m. p. 248° (effervescence) after crystallisation from methanol (Found: C, 31·3; H, 3·4. $C_{16}H_{18}I_2As_2$ requires C, 31·3; H, 3·0%).

The dibromide (IX), when heated at 0·1 mm., effervesced smoothly; the colourless liquid residue solidified on cooling, and when recrystallised from ethanol–chloroform gave the dimethylarsanthren (III), m. p. and mixed m. p. 191—192·5°.

(*C*) A mixture of the arsanthren (III) (1·31 g.), ethylene dibromide (0·34 c.c., 1 mol.), and methanol (1·5 c.c.) was heated at 100° for 9 hr. in a sealed tube which was occasionally shaken vigorously. Recrystallisation of the product from methanol yielded solvated *s-ethylenebis-5-(5 : 10-dihydro-5 : 10-dimethylarsanthronium) dibromide* (X), (0·80 g., 47%), m. p. 195° (effervescence) (Found: C, 41·9; H, 4·1; Br, 17·1. $C_{30}H_{32}Br_2As_4,2CH_4O$ requires C, 42·1; H, 4·2; Br, 17·5%). Concentration of the earlier mother-liquors furnished the dibromide (IX), m. p. 272° (effervescence) alone and mixed, in low yield.

The *dipicrate* (as X) separated from methanol in yellow crystals, m. p. 237° (decomp.) (Found: C, 44·15; H, 3·3; N, 7·2. $C_{42}H_{36}O_{14}N_6As_4$ requires C, 43·8; H, 3·3; N, 7·3%). The *di-iodide dihydrate* (from methanol) had m. p. 185° (effervescence) (Found: C, 36·9; H, 3·75. $C_{30}H_{32}I_2As_4,2H_2O$ requires C, 36·7; H, 3·5%).

The dibromide (X) (0·60 g.) was heated at 0·1 mm. for 5 min. in a hard-glass tube at 210°. Smooth effervescence occurred, and on cooling and recrystallisation from ethanol–chloroform the residue gave pale yellow mixed crystals (0·39 g., 76%), m. p. 142—147°, of the dimethyl derivative (III) and the 5-bromo-derivative (VII) in equimolecular proportions (Found: C, 44·7; H, 3·45. Calc. for $C_{14}H_{14}As_2 + C_{13}H_{11}BrAs_2$: C, 44·45; H, 3·4%). The following evidence confirms this composition. (*a*) A mixture of equimolecular amounts of (III) and (VII) was dissolved in hot chloroform, which was diluted with ethanol and cooled. Pale yellow crystals were deposited, of m. p. 142—147°, unchanged by admixture with the above product, and also by recrystallisation from acetone. (*b*) A solution of the above product in an excess of methyl iodide was boiled under reflux for 4 hr., a pale orange deposit being formed. Fractional recrystallisation of this from ethanol separated it into the less soluble arsanthren dimethiodide (as IV), deep orange crystals, m. p. 214° (decomp.) (Found: C, 28·85; H, 2·6%), and the more soluble 5 : 10-dihydro-5 : 10-dimethylarsanthren monomethiodide, m. p. 222° (effervescence) (Found: C, 37·9; H, 3·8%). Both m. p.s were unchanged on admixture with authentic samples. It is clear therefore that these two products are formed from (VII) and (III) respectively.

Reaction of the Arsanthren (III) *with Trimethylene Dibromide.*—A mixture of the powdered arsanthren (III) (1·55 g.) and the dibromide (0·476 c.c., 1 mol.) was heated at 155—160° for 1·5 hr., and the cold stone-hard product, when recrystallised from methanol, furnished the dihydrated 1 : 4-*dimethyltrimethylenedi-o-phenylenediarsonium dibromide* (XII) (1·05 g., 52%), m. p. 267—268° (effervescence) (Found: C, 35·75; H, 4·3. $C_{17}H_{20}Br_2As_2,2H_2O$ requires C, 35·8; H, 4·25%). It formed a *dipicrate*, yellow crystals, m. p. 252° (decomp.) from acetic acid (Found: C, 42·3; H, 2·95; N, 10·1. $C_{29}H_{24}O_{14}N_6As_2$ requires C, 42·0; H, 2·9; N, 10·1%).

The dibromide (XII) (0·25 g.) when heated at 0·1 mm., underwent the normal smooth decomposition with effervescence, and the residue, after cooling and solidifying, afforded the

arsanthren (III), m. p. and mixed m. p. 191—192·5° after crystallisation from ethanol–chloroform (Found : C, 50·9; H, 3·85%) : 0·13 g., 82% yield.

Reaction of the Arsanthren (III) *with o-Xylylene Dibromide.*—(*A*) A powdered mixture of the arsanthren (1·10 g.) and the dibromide (0·875 g., 1 mol.) was heated at 160° for 2 hr. and the hard solid product was then recrystallised from much ethanol, two fractions being isolated. The less soluble fraction, when further recrystallised from ethanol, afforded *5 : 5′-10 : 10′-bis-o-xylylenebisarsanthronium tetrabromide* (XIII), cream-coloured crystals (0·73 g., 39%), m. p. 273° (decomp.) (Found : C, 42·8; H, 3·0; Br, 28·5. $C_{40}H_{32}Br_2As_4$ requires C, 42·4; H, 2·8; Br, 28·2%). The more soluble fraction, when recrystallised from methanol, and dried at 70°/0·1 mm., furnished *di-o-phenylene-o-xylylenediarsine monomethobromide* (XIV) (0·33 g., 20%), m. p. 200° (Found : C, 50·1; H, 3·85. $C_{21}H_{19}BrAs_2$ requires C, 50·3; H, 3·8%). A sample of this salt (XIV), slowly crystallised from methanol–ethanol to obtain suitable crystals for *X*-ray examination (see below) separated apparently as a dimethanol solvate or a monohydrated monoethanol solvate (Found : C, 49·0, 48·8; H, 5·1, 4·7. $C_{21}H_{19}BrAs_2,2CH_4O$ requires C, 48·9; H, 4·8%).

Repetition of this experiment, but with heating at 130° for 1 hr., gave the tetrabromide (XIII), m. p. 273° (decomp.), in 8% yield, and the monobromide (XIV), m. p. 200°, in 65% yield.

(*B*) A mixture of the arsanthren (III) (1·65 g.) and the dibromide (2·60 g., 2 mols.) was heated at 160° for 2 hr. Recrystallisation of the product from methanol afforded solely the tetrabromide (XIII), m. p. 273° (decomp.) (1·80 g., 64%).

Derivatives of the Tetrabromide (XIII).—The addition of this salt to an excess of sodium iodide, both in cold methanol, precipitated the *tetra-iodide*, deep orange crystals, m. p. 244° (decomp.) from methanol (Found : C, 36·4; H, 2·1. $C_{40}H_{32}I_4As_4$ requires C, 36·3; H, 2·4%).

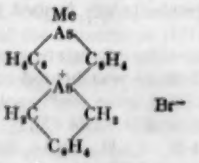
The yellow tetrapicrate was similarly deposited from methanolic sodium picrate solution, and when collected, washed with water, and dried in a vacuum at room temperature for 24 hr. formed a *decahydrate*, m. p. 232° (decomp.) (Found : C, 40·3; H, 3·5; N, 8·7. $C_{64}H_{40}O_{38}N_{12}As_4,10H_2O$ requires C, 40·3; H, 3·25; N, 8·8%). Attempted dehydration of this salt caused the colour to change to orange, and the substance became very hygroscopic; the pure anhydrous salt could not be obtained. Attempted recrystallisation from methanol caused decomposition.

Derivatives from, and Reactions of, the Monobromide (XIV).—The corresponding *picrate*, prepared and recrystallised in ethanol, formed yellow crystals, m. p. 211° (Found : C, 49·6; H, 3·7; N, 6·3. $C_{27}H_{21}O_7N_3As_2$ requires C, 49·9; H, 3·3; N, 6·45%). The *iodide*, when recrystallised from methanol, had m. p. 197° (Found : C, 46·0; H, 3·8. $C_{21}H_{19}IAs_2$ requires C, 46·0; H, 3·5%).

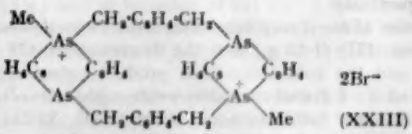
The monobromide (XIV), when heated at 0·1 mm., underwent decomposition with slight effervescence, and the yellow residual liquid on cooling formed a glass containing some apparently crystalline material. No crystalline constituent could be isolated, however, in spite of the use of a variety of solvents.

A mixture of the monobromide (XIV) (0·60 g.) and *o*-xylylene dibromide (0·32 g., 1 mol.) was heated at 140—145° for 2 hr., but did not solidify completely until cold. Recrystallisation from methanol afforded the tetrabromide (XIII) (0·45 g., 66%), m. p. 273° (decomp.), alone and mixed (Found : C, 42·7; H, 2·6%).

Structure of the Monobromide (XIV).—The following report by Dr. W. Schaffer indicates solely the main points by which the essential structure has been determined, with particular reference to the possible alternatives (XXII) and (XXIII; Me groups *cis* or *trans*). The full crystallographic data will be published elsewhere.



(XXII) Br^-



$2Br^-$ (XXIII)

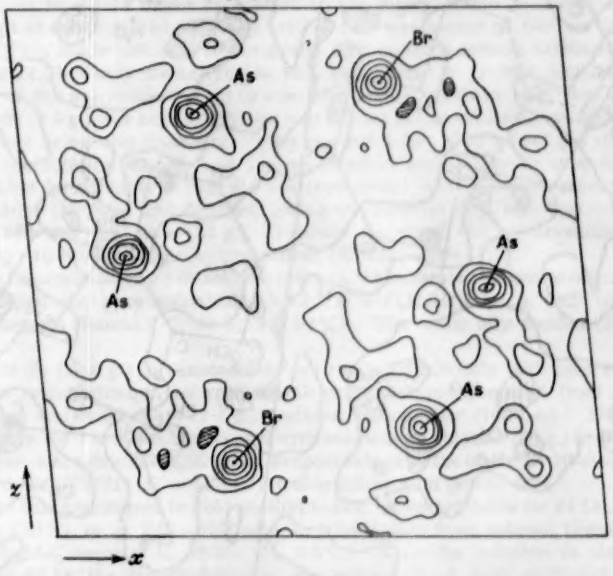
" The immediate object of this investigation was to find the positions of the heavy atoms and (if possible) the benzene rings, rather than to determine bond lengths and angles accurately, in order to eliminate two of the three possible structures.

" *Crystallographic data.* From oscillation photographs and Weissenberg photographs using copper K_α radiation, together with optical measurements of the angles between pairs of faces in a zone, it was found that the crystal was triclinic and the unit cell had the dimensions: $a = 12{\cdot}4$, $b = 7{\cdot}8$, $c = 12{\cdot}0$ Å; $\alpha = 107°$, $\beta = 93°$, $\gamma = 92°$: $a^* = 0{\cdot}127$, $b^* = 0{\cdot}205$, $c^* = 0{\cdot}132$; $\alpha^* = 72°$, $\beta^* = 83°$, $\gamma^* = 86°$. $V = 1110$ Å^3. The crystals have d 1·55, giving 2 molecular units per unit cell.

" By using intensities of reflexions from the (010) projection in the Wilson statistical method (Howells, Phillips, and Rogers, *Acta Cryst.*, 1950, **3**, 210), the crystal was found to be centrosymmetric, space group $P\bar{1}$.

" The signs of the larger unitary structure factors were found by a direct method, based on Harker–Kasper inequalities and a criterion suggested by Cochran and Douglas (unpublished). Electron-density maps then showed clearly the positions of the arsenic and the bromine atoms, in projection on (100) and (010) (see Fig. 1). A ' difference ' density map, from which these

FIG. 1. (010) *Fourier projection. Contour scale arbitrary.*



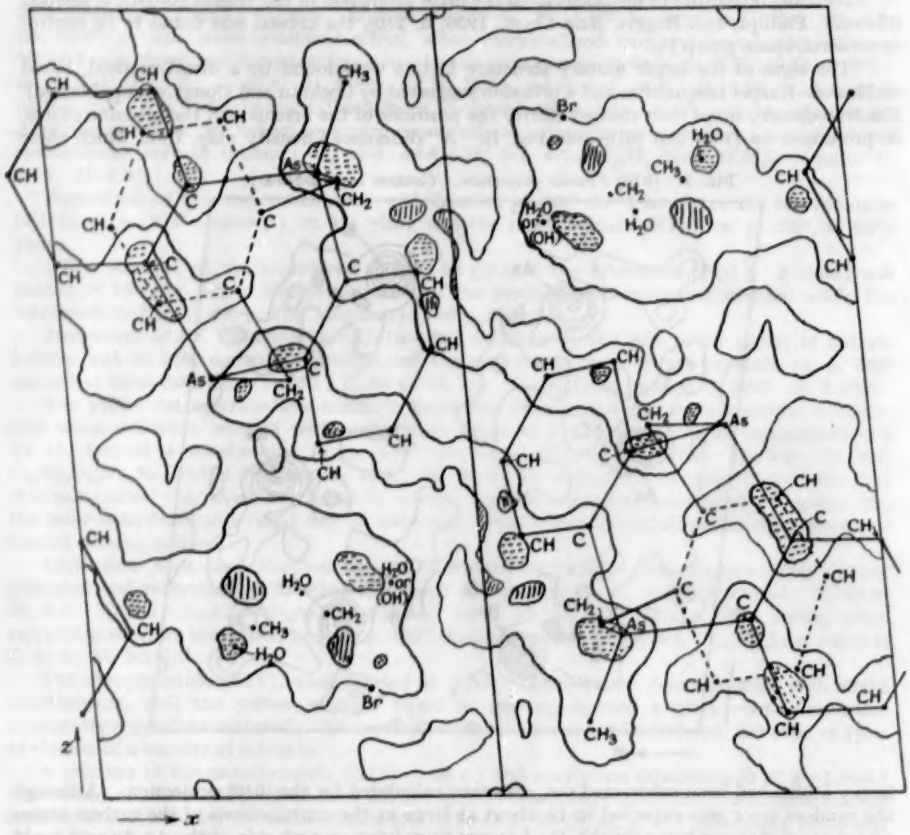
heavy atoms had been subtracted out, was then calculated for the (010) projection. Although the random error was expected to be about as large as the contributions of the carbon atoms whose positions were being sought, the benzene rings lying on each side of the As–As axis could be seen (Fig. 2). No decisive indication of the positions of the remaining carbon atoms was found, however, from this map. The positions finally chosen for them were arrived at by the following packing considerations, and are in good agreement with Fig. 2.

" Wire models of the structures (XIV), (XXII), and (XXIII) were constructed, and attempts made to fit each in turn into the electron-density maps. The structure (XXIII) could be immediately ruled out. The structure (XIV) accounted best for the peaks in the ' difference ' map; the distances between atoms of adjacent molecules were satisfactory, and no serious distortion of bond angles was involved.

" There remained one fairly large cavity between the main molecules into which molecules of solvent of crystallisation could be fitted. The crystals used for the *X*-ray work had separated from methanol–ethanol containing a trace of water. In agreement with their analytical composition (p. 418), two molecules of methanol per molecular unit were tried in the model, but no positions were found which did not imply improbably small values of some interatomic distances. One molecule of ethanol plus one of water per molecular unit were then tried, but again, although this could not be regarded as impossible, some of the distances involved between carbon atoms of different molecules (a little less than 3·5 Å) were too small to make the arrangement probable.

It was then found that ethanol fitted in, with interatomic distances nearer to accepted values. Furthermore, three molecules of water fitted fairly well into the cavity in the unit cell. A statistical distribution of one ethanol and three water molecules among the available cavities in the structure, about three cavities containing ethanol to each one containing water, would

FIG. 2. (010) *Difference map. Contour scale arbitrary. Horizontal hatching indicates a peak of high electron density, vertical hatching indicates a lower density area.*


CH
CH
CH

in the Table. Atomic co-ordinates for atoms in the solvent molecules of crystallisation are not included in this Table."

5 : 10-Dihydro-2 : 5 : 10-trimethylarsanthren (XVIII; R = Me) *and its Derivatives.*—A solution of *o*-arsanilic acid (XV) (64 g.) in water (600 c.c.), mixed with concentrated hydrochloric acid (88 c.c.), was diazotised at 0° by the slow addition of a solution of sodium nitrite (20 g.), and then run slowly into vigorously stirred ice-water (1 l.) concurrently with a solution of dichloro-*p*-tolylarsine (78 g., 1·1 mols.) in aqueous 5N-sodium hydroxide (280 c.c.) and N-sodium carbonate (240 c.c.). The mixture was set aside overnight, then diluted with water (1 l.) and heated to 100°, and concentrated hydrochloric acid was cautiously added until precipitation of *p*-tolylarsenoxide was complete. The filtered solution was reheated, and made just acid to Congo-red by further addition of acid, the *anhydride* (XVI; R = C_6H_4Me) (80 g., 68%) of *o*-arsonophenyl-*p*-tolylarsinic acid being precipitated as a microcrystalline powder, m. p. 380° (decomp.); it was purified by boiling its solution in aqueous sodium carbonate (charcoal), and reprecipitating it with acetic acid, and formed a colourless powder, m. p. 382—383° (decomp.) (Found: C, 40·9; H, 2·95. $C_{13}H_{13}O_4As_2$ requires C, 40·85; H, 3·1%).

In an attempt to obtain direct cyclisation to the *p*-tolyl group, a stirred solution of this anhydride (1 g.) in concentrated sulphuric acid (5 c.c.) was heated at 100° for 20 min., poured into water (30 c.c.), made just acid to Congo-red with aqueous sodium carbonate, and concentrated to *ca.* 50 c.c., but only the anhydride, m. p. and mixed m. p. 380° (decomp.), separated.

A solution of the anhydride (80 g.) in concentrated hydrochloric acid (800 c.c.) containing potassium iodide (0·5 g.) was kept at 100° for 8 hr. whilst sulphur dioxide was passed through it, hydrogen chloride being also passed in during the last 2 hr. The mixed gas stream was continued whilst the solution cooled, and the supernatant aqueous layer then decanted. The heavy oily residue (presumably XVII) did not crystallise; its solution in chloroform (350 c.c.) was therefore dried (Na_2SO_4) and distilled, giving fractions (*a*) b. p. 92—188°/0·05 mm. (13 g.) and (*b*) b. p. 188—193°/0·05 mm. (35 g.). Fraction (*b*), which did not crystallise, was impure 5 : 10-dichloro-5 : 10-dihydro-2-methylarsanthren (XVIII; R = Cl).

A solution of fraction (*b*) (1 g.) in acetone (10 c.c.), when treated dropwise with 30% hydrogen peroxide, deposited the pure anhydride (XVI; R = C_6H_4Me), m. p. 382° (decomp.) when washed with acetone (Found: C, 40·6; H, 3·1%). The crude oily residue (XVII) behaved similarly.

A solution of (*b*) (10·8 g.) in benzene (40 c.c.) reacted vigorously with heat evolution when added dropwise under nitrogen to a stirred Grignard reagent prepared from methyl iodide (9·5 c.c., 6 mols.) and magnesium (3·7 g., 6 atoms) under ether (100 c.c.). The mixture was boiled under reflux for 1 hr., and hydrolysed with ammonium chloride (25 g.) in water (100 c.c.). The organic layer, when dried (Na_2SO_4) and evaporated, gave the crude 5 : 10-dihydro-2 : 5 : 10-trimethylarsanthren (XVIII; R = Me) as a foul-smelling gum (8·6 g., 90%).

A solution of this arsanthren in cold methyl iodide, when set aside for 24 hr., deposited the *monomethiodide* (XIX), m. p. 215—216° after crystallisation from ethanol (Found: C, 39·05; H, 4·15. $C_{16}H_{19}IAs_2$ requires C, 39·35; H, 3·9%). A similar solution in methyl bromide deposited during 48 hr. the dimethobromide, which crystallised from methanol as the *monohydrate*, m. p. 265° (effervescence) (Found: C, 37·2; H, 4·3. $C_{17}H_{22}Br_2As_2,H_2O$ requires C, 36·9; H, 4·3%); it gave a *dimethopicrate*, yellow crystals, m. p. 258° (decomp.) from ethanolic dimethylformamide (Found: C, 42·1; H, 3·4; N, 10·2. $C_{29}H_{26}O_{14}N_6As_2$ requires C, 41·8; H, 3·1; N, 10·1%).

When equimolecular mixtures of the arsanthren (XVIII; R = Me) and ethylene or trimethylene dibromide were set aside for several days, or their methanolic solutions were boiled, no apparent reaction occurred and the foul odour of the arsanthren persisted. When the mixtures were heated at 100°, an odourless hygroscopic gum was readily formed, but this product, and its iodide and picrate, could not be obtained crystalline.

5 : 10 : 5′ : 10′-Tetrahydro-2 : 5 : 10 : 2′ : 5′ : 10′-hexamethyl-5 : 5′-10 : 10′-bis-o-xylylenebisarsanthronium Tetraiodide (XX).—A mixture of (XVIII; R = Me) (4·2 g.) and powdered *o*-xylylene dibromide (3·2 g., 1 mol.) was heated at 100° for 1·5 hr., and the highly hygroscopic product, dissolved in ethanol (50 c.c.), was then added to a solution of sodium iodide (8 g.) in ethanol (60 c.c.). The precipitated tetraiodide, recrystallised from methanol, gave the *monohydrate* (6 g., 70%), m. p. 180—181° (decomp.) (Found: C, 38·8; H, 3·9. $C_{46}H_{46}I_4As_4,H_2O$ requires C, 38·75; H, 3·5%); this gave a *tetrapicrate*, yellow crystals, m. p. 171—173° (from aqueous methanol) (Found: C, 46·05; H, 3·3; N, 8·9. $C_{70}H_{56}O_{28}N_{12}As_4$ requires C, 46·3; H, 3·1; N, 9·25%).

When the tetraiodide was heated at 170°/0·1 mm. for 30 min., decomposition with

effervescence occurred, but the yellow gummy residue on attempted recrystallisation gave only an oil, which did not yield a solid methiodide.

The tetraiodide gave a *tetra-(+)-bromocamphorsulphonate dihydrate*, m. p. 257—258° (decomp.) from acetone (Found: C, 47·4; H, 5·2. $C_{56}H_{104}O_{16}Br_4S_4As_4.2H_2O$ requires C, 47·4; H, 5·1%). Further recrystallisation did not change the m. p.; the salt, after two and three recrystallisations, had $[M]_D$ +1104° and +1110° respectively in aqueous solution; the value expected for four sulphonate radicals is $[M]_D$ +1112°.

The *tetra[antimony -tartrate] dihydrate* (from aqueous ethanol) had m. p. 239° (effervescence) (Found: C, 37·9; H, 3·4. $C_{44}H_{56}O_{34}As_4Sb_4.2H_2O$ requires C, 37·5; H, 3·25%), $[M]_D$ +1648°; the m. p. and rotation were unaffected by three recrystallisations, and then gave an inactive iodide and picrate.

The (+)-tartrate, (+)-camphorsulphonate, and (−)-*N*-1-phenylethylphthalamate were obtained only as very hygroscopic products.

The Anhydride (XVI; R = C_6H_4OMe) *of o-Arsonophenyl-p-methoxyphenylarsinic Acid.*—Diazotised *o*-arsanilic acid, when treated with *p*-methoxyphenylarsenoxide as described for (XVI; R = C_6H_4Me), gave this *anhydride* (51%), m. p. 373° (decomp.) after washing with hot water and acetone (Found: C, 38·85; H, 3·45. $C_{13}H_{12}O_5As_2$ requires C, 39·2; H, 3·05%). Treatment with hot sulphuric acid, as described above, again yielded the unchanged anhydride. Treatment with hot hydrochloric acid and sulphur dioxide gave ultimately a heavy oil which solidified, and when recrystallised from *cyclo*hexane (charcoal) gave the oxychloride (XXI) (84%), yellow crystals, m. p. 148—150° (Found: C, 23·4; H, 1·1. Calc. for $C_6H_4OCl_2As_2$: C, 23·0; H, 1·3%).

Diazotised *o*-arsanilic acid, when similarly treated with dichloro-*p*-nitrophenylarsine, gave, on final acidification to Congo-red, a precipitate of a *diarsonoazobenzene* as a white microcrystalline powder, m. p. >450° after crystallisation from much water (Found: C, 33·0; H, 2·7; N, 6·8. $C_{12}H_{10}O_6N_2As_2$ requires C, 33·4; H, 2·8; N, 6·5%). Treatment with hydrochloric acid and sulphur dioxide gave a heavy oil which solidified on cooling, and when recrystallised from benzene–*cyclo*hexane (1 : 1) gave the *bis(dichloroarsino)azobenzene* (78%), yellow crystals, m. p. 129—131° (Found: C, 30·6; H, 2·0; N, 5·8. $C_{12}H_8N_2Cl_4As_2$ requires C, 30·5; H, 1·7; N, 5·9%).

The orientation of the arsenic groups in the above compounds is uncertain, but we suggest that they are in the *op'*-positions, which their synthesis renders probable. Karrer (*Ber.*, 1912, **45**, 2359) describes the *pp'*-diarsonoazobenzene as a dull brown powder (no m. p. recorded); Kalb (*loc. cit.*) and Lieb (*Ber.*, 1921, **54**, 1511) describe the *oo'*-isomer, m. p. 272°, and the *mm'*-isomer, m. p. 240° (decomp.), as orange-yellow and deep orange-yellow respectively. The recorded colours of these compounds may not be those of the pure compounds. Moreover, the strongly acidic arsono-groups may considerably suppress the resonance to which the normal colours of azo-compounds are due, and the fact that our diarsono-compound is colourless does not preclude its having the azo-structure.

We are greatly indebted to Dr. W. Schaffer for the *X*-ray crystal investigation, to Dr. A. G. Maddock for arsenic estimations by activation analysis, and to the Department of Scientific and Industrial Research for a grant (E. R. H. J.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, September 6th*, 1954.]

1 : 2-*Dicarboxylic Acids. Part IV.* Saturated and Unsaturated Dialkyl- and Alkyl-aryl-dinitriles.*

By W. F. Beech and H. A. Piggott.

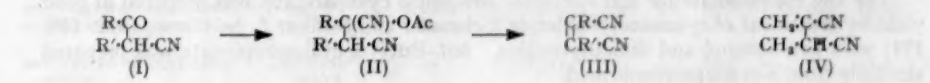
[Reprint Order No. 5751.]

Dialkyl and alkyl-aryl derivatives of maleic and fumaric dinitriles, which are key intermediates for syntheses of metallic tetrazaporphins, have been prepared in excellent yields by pyrolysis of the cyanohydrin acetates of β-keto-nitriles.† The *cis*- and *trans*-stereoisomers have been separated and characterised by measurement of their dipole moments.

A general method for preparing αβ-dialkyl- and β-alkyl-α-phenyl-succinonitriles depending on the thermal instability of *tert.*-butyl α-alkyl-αβ-dicyanobutyrate and α-alkyl-αβ-dicyanophenylpropionate respectively is described. The latter compounds were obtained in good yields by an extension of Higson and Thorpe's method (*J.*, 1906, **89**, 1462).

The importance of maleinitrile and of alkyl derivatives of this nitrile and fumaronitrile as intermediates for syntheses of metallic tetrazaporphins has recently been demonstrated (Linstead and Whalley, *J.*, **1952**, 4839; France, Jones, and Imperial Chemical Industries Limited, B.P. 688,768, 689,387, 689,389), but investigation of the new pigments has hitherto been restricted by inaccessibility of many of the necessary intermediates. Although methods have been described for the preparation of maleinitrile by Linstead and Whalley (*loc. cit.*) and of 3 : 4 : 5 : 6-tetrahydrophthalonitrile by Ficken and Linstead (*J.*, 1952, 4846), yet the simple dialkyl and alkyl-aryl derivatives of fumaric and maleic dinitriles have hitherto proved extremely difficult to obtain, even in small quantities. Analogous succinonitrile derivatives, which are potentially useful intermediates (Elvidge and Linstead, *J.*, 1954, 442), were also inaccessible because the usual methods for making the parent compound failed when applied to its αβ-dialkyl derivatives.

The present investigation has shown, however, that dinitriles of the unsaturated series (III) are best obtained by pyrolysis of the cyanohydrin acetates (II) of β-keto-nitriles. The β-keto-nitriles (I) required for this synthesis were obtained by dimerisation of aliphatic



nitriles in the presence of sodium, with subsequent alkylation and hydrolysis (Mohr, *J. pr. Chem.*, **1914**, **90**, 195), or by the new method described below. Aryl-substituted β-keto-nitriles (I; R′ = aryl) were made by condensation of phenylacetonitriles with esters in the presence of sodium ethoxide (*Org. Synth.*, Coll. Vol. II, 1943, p. 487). The cyanohydrins of these keto-nitriles are unstable, even at ordinary temperatures. When treated with a mixture of thionyl chloride and pyridine, they gave very poor yields (*ca.* 10%) of unsaturated dinitriles (III). By pyrolysis of the more stable cyanohydrin acetates (II) at 470—490°, however, the dimethyl (III; R = R′ = Me), ethylmethyl (III; R = Me, R′ = Et), phenyl (III; R = H, R′ = Ph), methylphenyl (III; R = Me, R′ = Ph), and benzylmethyl (III; R = Me, R′ = CH_2Ph) derivatives of fumaric and maleic dinitriles were prepared in yields of approximately 90%. The product of pyrolysis usually consisted of a mixture of *cis*- and *trans*-forms of type (III); these were separated by fractional distillation, and characterised by measurement of their dipole moments, the *cis*-forms possessing moments of approx. 6 D, and the *trans*-forms much lower moments, usually well below 2 D. The possibility that some of these compounds might possess the alternative, itacononitrile, type of structure (*e.g.*, IV) appeared from spectrometric results to be unlikely. In particular, the bands in the region 940—950 cm.$^{-1}$, which would be expected if the structure CH_2:C(CN)·CHR·CN was present (Kitson, *Analyt. Chem.*, 1953, **25**, 1470), were not observed.

* Part III, Ficken, France, and Linstead *J.*, 1954, 3730. † Patent protection pending.

A by-product obtained from the pyrolysis of 2-acetoxy-2 : 3-dicyanopentane (II; R =Me, R′ = Et), appeared, however, to be αγ-dimethylitacononitrile, as it gave the corresponding acid on hydrolysis.

Attempts to prepare αβ-dimethylsuccinonitrile by the methods generally used for making succinonitrile were unsuccessful. Treatment of 2 : 3-dichloro- or 2 : 3-dibromobutane with metallic cyanides under a variety of conditions afforded none of the required dinitrile; only tars, unsaturated compounds, and unchanged halogenobutanes were isolated. α-Methylcrotononitrile proved very unreactive towards hydrogen cyanide in the presence of basic catalysts, and gave only traces of αβ-dimethylsuccinonitrile, even under drastic conditions. This was not unexpected in view of the results obtained by Kurtz (*Annalen*, 1951, **572**, 23) when attempting to add hydrogen cyanide to crotononitrile.

The reaction between cyanohydrins and ethyl sodiocyanoacetate, first described by Higson and Thorpe (*loc. cit.*), appeared to provide the basis of a general method for the synthesis of alkyl- and aryl-succinonitriles. Attempts to prepare αβ-dimethylsuccinonitrile (VII; R′ = Me) by partial hydrolysis and decarboxylation of ethyl αβ-dicyano-α-methylbutyrate (VI; R = Et, R′ = Me), however, gave only small yields of the dinitrile (Linstead and Whalley, *J.*, 1954, 3722). As the low yield of dinitrile obtained by Linstead and Whalley appeared to be due, at least in part, to side reactions during the partial

$$\mathrm{Me{\cdot}CH(CN){\cdot}OH + CH_2(CN){\cdot}CO_2R \longrightarrow Me{\cdot}CH(CN){\cdot}CH(CN){\cdot}CO_2R \longrightarrow}$$
(V)

$$\mathrm{Me{\cdot}CH(CN){\cdot}CR'(CN){\cdot}CO_2R \longrightarrow Me{\cdot}CH(CN){\cdot}CHR'{\cdot}CN}$$
(VI) (VII)

hydrolysis, it seemed desirable to use in place of the ethyl ester one which could be dealkylated by some method other than hydrolysis. Possibilities included the benzyl ester (Bowman, *J.*, 1950, 325), the tetrahydropyran-2-yl ester (Bowman and Fordham, *J.*, 1952, 3945) and the *tert.*-butyl ester (Breslow, Baumgarten, and Hauser, *J. Amer. Chem. Soc.*, 1944, **66**, 1286; Fonken and Johnson, *ibid.*, 1952, **74**, 831); in practice, the *tert.*-butyl ester gave excellent results and proved easy to manipulate on account of the convenience of *tert.*-butanol as a solvent. Troublesome ester interchanges which were encountered, for example, when using the benzyl ester in ethanol were thus avoided.

The key intermediate for this synthesis, *tert.*-butyl cyanoacetate, was prepared in good yield by treatment of cyanoacetyl chloride (Schroeter and Seidler, *J. pr. Chem.*, 1922, **105**, 171) with *tert.*-butanol and dimethylaniline. *tert.*-Butyl α-cyanopropionate was prepared similarly from α-cyanopropionic acid.

tert.-Butyl cyanoacetate with acetaldehyde cyanohydrin in the presence of sodium *tert.*-butoxide afforded *tert.*-butyl sodio-αβ-dicyanobutyrate (in almost quantitative yield), which with methyl iodide and with benzyl chloride gave high yields of *tert.*-butyl α-methyl- (VI; R = Bu^t, R′ = Me) and α-benzyl-αβ-dicyanobutyrate (VI; R = Bu^t, R′ = CH_2Ph), respectively. These esters decomposed when heated, especially under slightly acid conditions, to give αβ-dimethyl- (VII; R′ = Me) and α-benzyl-β-methyl-succinonitrile (VII; R′ = CH_2Ph), respectively, together with *iso*butylene and carbon dioxide. The best yields (81% and 89%) of dinitriles were obtained by dropping the *tert.*-butyl esters, mixed with some acetic acid, on silica at 200—210°. When *tert.*-butyl αβ-dicyano-α-methylbutyrate was heated at 180° with 2% of toluene-*p*-sulphonic acid in a flask, lower yields of dimethylsuccinonitrile were obtained together with a considerable amount of α-cyano-αβ-dimethylsuccinimide formed by interaction of the cyano- and the carboxyl group of the intermediate αβ-dicyano-α-methylbutyric acid (cf. König, *J. pr. Chem.*, 1904, **69**, 1). The formation of this compound explains why poor yields of dimethylsuccinonitrile were obtained by distillation of the acid, *i.e.*, high yields of dinitrile result only when the free acid is liberated at a temperature sufficiently high to effect its rapid decarboxylation. In this connection it is noteworthy that *tert.*-butyl αβ-dicyanobutyrate (VI; R = Bu^t, R′ = H), which evolves *iso*butylene at much lower temperatures than its α-methyl derivative, gave a very poor yield of methylsuccinonitrile on pyrolysis.

In preparing phenylsuccinonitrile and α-methyl-β-phenylsuccinonitrile, benzaldehyde

was condensed with *tert.*-butyl cyanoacetate in the presence of piperidine, and the product was treated with sodium cyanide. The resulting *tert.*-butyl αβ-dicyano-β-phenylpropionate decomposed when heated to phenylsuccinonitrile. Methylation of the sodio-derivative of the former yielded *tert.*-butyl αβ-dicyano-α-methyl-β-phenylpropionate which afforded α-methyl-β-phenylsuccinonitrile on pyrolysis.

In the synthesis just described, two common reactions of ethyl cyanoacetate (Knoevenagel condensation and Higson–Thorpe condensation with cyanohydrins) were applied to the *tert.*-butyl ester. Several other possibilities were envisaged, but only the synthesis of β-keto-nitriles, of special importance in the present investigation, was examined. Treatment of *tert.*-butyl sodio-α-cyanopropionate with acetyl chloride afforded *tert.*-butyl α-cyano-α-methylacetoacetate (VIII). Pyrolysis of the latter at 220—230° gave a good yield of α-acetylpropionitrile (IX), thus providing an alternative to the method of Mohr (*loc. cit.*) for making the β-keto-nitriles required as intermediates for alkylmaleic and alkylfumaric dinitriles :

$$Me{\cdot}CH(CN){\cdot}CO_2Bu^t + Me{\cdot}COCl \longrightarrow \underset{(VIII)}{Me{\cdot}CO{\cdot}CMe(CN){\cdot}CO_2Bu^t} \longrightarrow \underset{(IX)}{Me{\cdot}CO{\cdot}CHMe{\cdot}CN}$$

Experimental

Preparation of Cyanohydrin Acetates of β-Keto-nitriles.—The ketonitrile (1 mol.) was added gradually with stirring to a mixture of anhydrous hydrogen cyanide (100 c.c.; 2·5 mols.) and potassium hydroxide (10 pellets; *ca.* 1 g.) at 0—5°; after 15—20 hours' stirring, the mixture was kept at 10—15° for 1 hr. and then cooled again to 5°. Sulphuric acid (25 drops; *d* 1·84) was added, and excess of hydrogen cyanide distilled off under reduced pressure (bath-temp. 50—60°). The residue, which consisted of the unstable cyanohydrin, was treated immediately with acetic anhydride (210 c.c.) and sulphuric acid (21 drops). After the mixture had been heated for 2 hr. on the steam-bath, the cyanohydrin acetate (Table 1) was isolated by fractional distillation. Yields averged 90—95% of theory.

Table 1. *Physical properties and analyses of cyanohydrin acetates of β-keto-nitriles.*

Keto-nitrile	Cyanohydrin acetates B. p./mm.	n_D^{20}	Formula	Found, % C	H	N	Required, % C	H	N
α-Methylacetoacetonitrile [1]	95°/0·7	1·4362	$C_8H_{10}O_2N_2$	58·0	6·0	16·7	57·85	6·0	16·85
α-Ethylacetoacetonitrile [1]	98—100°/0·9	1·4395	$C_9H_{12}O_2N_2$	60·5	6·3	15·5	60·0	6·65	15·55
α-Formyl-α-phenylacetonitrile [2]	138—140°/0·07 [3]	—	$C_{12}H_{10}O_2N_2$	—	—	13·2	—	—	13·1
α-Phenylacetoacetonitrile [4]	120°/0·03	(m. p. 74—84°) [5]	$C_{12}H_{12}O_2N_2$	68·1	5·5	12·4	68·4	5·25	12·3
α-Benzylacetoacetonitrile [1]	158°/0·04	(m. p. 103—104°)	$C_{14}H_{14}O_2N_2$	69·4	5·8	11·5	69·4	5·8	11·55

[1] Mohr, *J. pr. Chem.*, 1914, **90**, 189. [2] Ghosh, *J.*, 1916, **109**, 113. [3] This compound gave some unsaturated dinitrile during prolonged distillation. [4] *Org. Synth.*, Coll. Vol. II, 1943, p. 487. [5] Mixture of stereoisomers.

Table 2. *Pyrolysis of cyanohydrin acetates of β-keto-nitriles.*

Compound pyrolysed	Wt. (g.)	Acetic acid (c.c.)	Yield of mixed dinitriles Wt. (g.)	%	Approx. ratio, *trans* : *cis*
2-Acetoxy-2 : 3-dicyanobutane	291	333	169	91	3 : 1
2-Acetoxy-2 : 3-dicyanopentane	121·3	130	64·7	80	2 : 1
2-Acetoxy-1 : 2-dicyano-1-phenylethane	36	35	23·2	90	1 : 1
2-Acetoxy-1 : 2-dicyano-1-phenylpropane	100	85	63·8	87	7 : 1
3-Acetoxy-2 : 3-dicyano-1-phenylbutane	72·6	103	45·8	84	20 : 1

Preparation of Substituted Maleic and Fumaric Dinitriles by Pyrolysis of Cyanohydrin Acetates.—A solution (Table 2) of the cyanohydrin acetate in acetic acid was introduced dropwise (2—2·5 c.c./min.) into an inclined pyrolysis tube (90 × 2·5 cm.) packed with pieces of silica and kept at 470—490° (internal thermocouple) by means of an electric tube furnace (1 kw). The volatile products were condensed in a receiver cooled by ethanol–solid carbon dioxide. The tube

was afterwards purged of residual products by passage of acetic acid (100 c.c.) and then nitrogen The dinitriles were isolated by fractional distillation. Separation of the *cis*- and the *trans*-forms (and, in some cases, of other isomers) was effected by fractional distillation under reduced pressure of the mixed dinitriles through a column packed with stainless-steel gauze rings. The individual fractions were further purified by crystallisation, usually from methanol or ethanol.

Pyrolysis of 2-acetoxy-2 : 3-dicyanopentane gave in addition to ethylmethyl-fumaro- and -malei-dinitriles (combined yield, 61%) an isomeric compound (19%), b. p. 61—63°/11 mm., which was not obtained quite pure (Found : C, 70·9; H, 6·6; N, 22·8. Calc. for $C_7H_8N_2$: C, 70·0; H, 6·65; N, 23·35%). Alkaline hydrolysis of this product gave an acid, m. p. 195° (decomp.). Fichter and Rudin (*Ber.*, 1904, **37**, 1617) give m. p. 202° (decomp.) for αγ-dimethyl-itaconic acid.

Pyrolysis of 3-acetoxy-2 : 3-dicyanophenylbutane gave a small amount (<5% of total product) of a *compound* of unknown constitution. After crystallisation from benzene, this had m. p. 80° (Found : C, 40·5, 40·7; H, 8·4, 8·7%).

Hydrolysis of the *nitriles* of phenylmaleic and phenylfumaric acid with hot, concentrated hydrochloric acid gave respectively phenylmaleic anhydride and phenylfumaric acid. The former, after crystallisation from carbon disulphide, had m. p. 119°. Alexander (*Annalen*, 1890, **258**, 77) gives m. p. 119—119·5° (Found : C, 69·0; H, 3·0. Calc. for $C_{10}H_6O_3$: C, 69·0; H, 3·45%). Phenylfumaric acid, after crystallisation from benzene, melted at 125—127°. Almström (*ibid.*, 1916, **411**, 375) gives m. p. 128—129°.

TABLE 3. *Physical properties and analyses of αβ-unsaturated dinitriles.*

Dinitrile	M. p.	B. p./mm.	Dipole moment, D [1]	Formula	Found, % C	H	N	Required, % C	H	N
Dimethylmaleic	48°	136—138°/21	6·0	$C_6H_8N_2$	67·9	5·4	26·3	67·9	5·65	26·4
Dimethylfumaric	81°	101—102°/55	0·7	$C_6H_8N_2$	67·9	5·9	26·1	67·9	5·65	26·4
Ethylmethylmaleic ...	(n_D^{20} 1·4671)	131—132°/12	5·5	$C_7H_8N_2$	69·5	6·3	22·9	70·0	6·65	23·35
Ethylmethylfumaric	(n_D^{20} 1·4613)	72—74°/12	1·4	$C_7H_8N_2$	69·5	6·8	23·2	70·0	6·65	23·35
Phenylmaleic	89—90°	115—118°/ 0·05	6·1	$C_{10}H_6N_2$	78·1	4·3	18·0	77·9	3·9	18·2
Phenylfumaric	42—43°	82—84°/0·2	1·9	$C_{10}H_6N_2$	77·7	3·8	17·9	77·9	3·9	18·2
Methylphenylmaleic	57°	110°/0·04	6·2	$C_{11}H_8N_2$	78·8	4·8	16·6	78·55	4·75	16·65
Methylphenylfumaric	70°	80—85°/0·05	1·2	$C_{11}H_8N_2$	78·3	5·0	17·1	78·55	4·75	16·65
Benzylmethylmaleic [2]	[Liquid]	137°/0·05	3·7	$C_{12}H_{10}N_2$	79·6	5·8	12·7	79·1	5·5	15·4
Benzylmethylfumaric	40°	90—92°/0·15	0·8	$C_{12}H_{10}N_2$	79·2	5·7	15·3	79·1	5·5	15·4

[1] Approximate values, in benzene solution at 30°. [2] Owing to the small quantity of material, benzylmethylmaleidinitrile was not obtained pure. Its infra-red spectrum showed a strong band at 1720 cm.$^{-1}$, indicating the presence of a carbonyl impurity (probably α-benzylacetoacetonitrile); this would explain the anomalous nitrogen analysis and dipole moment.

Acetaldehyde Cyanohydrin.—Acetaldehyde (110 g.) was added to a cooled mixture of anhydrous hydrogen cyanide (97 c.c.) and piperidine (2 g.) at 10—20°. After the mixture had been kept at 25° for 4 hr., it was treated with sulphuric acid (1 c.c.; *d* 1·84). Fractional distillation afforded acetaldehyde cyanohydrin (160 g.; 90%), b. p. 72—76°/7 mm., $n_D^{19\cdot2}$ 1·4041. Brühl (*Z. physikal. Chem.*, 1895, **16**, 214) gives $n_D^{18\cdot4}$ 1·4058.

tert.-*Butyl Cyanoacetate.*—Phosphorus pentachloride (417 g.) was added portionwise to a stirred solution of cyanoacetic acid (170 g.) in anhydrous ether (1 l.). The mixture was cooled occasionally to prevent excessive refluxing, and stirring was continued until the phosphorus pentachloride had dissolved completely. Most of the ether was then distilled from a bath at 50—60°, after which phosphoryl chloride was removed at 10—15 mm. (bath-temp. 50—65°), the receiver being cooled in ice–salt. The residue (205 g.) was added dropwise and without delay to a stirred solution of dry *tert.*-butanol (148 g.) and dimethylaniline (242 g.) in anhydrous ether (300 c.c.); the mixture was cooled occasionally to prevent excessive refluxing. After being boiled under reflux for 2 hr. and stored for 15 hr., the mixture was stirred with water (1 l.), and the ethereal layer separated. The latter was shaken with successive portions of 2N-sulphuric acid (500 c.c.) until free from dimethylaniline after which it was washed with 2N-sodium carbonate and dried ($MgSO_4$). After removal of the ether by distillation the residue

was treated with potassium carbonate (*ca.* 1 g.; anhyd.) and purified by distillation under reduced pressure (yield, 186 g., 66%; b. p. 90°/10 mm., 54—56°/0·3 mm., n_D^{20} 1·4198) (Found: C, 59·9; H, 7·9; N, 9·6. Calc. for $C_7H_{11}O_2N$: C, 59·6; H, 7·8; N, 9·95%).

tert.-*Butyl α-cyanopropionate* was prepared from α-cyanopropionic acid in a similar manner (yield 63%; b. p. 55°/0·3 mm., n_D^{20} 1·4138) (Found: C, 62·2; H, 8·6; N, 9·2. $C_8H_{13}O_2N$ requires C, 61·95; H, 8·4; N, 9·05%).

tert.-*Butyl αβ-Dicyanobutyrate* (V; R = Bu^t).—Sodium (17·3 g.), in small pieces, was boiled under reflux with *tert.*-butanol (750 c.c.) for 18 hr. The resulting suspension of sodium *tert.*-butoxide was cooled to 25° and *tert.*-butyl cyanoacetate (105·8 g.) was added with stirring, followed immediately by acetaldehyde cyanohydrin (53·3 g.). During addition of the latter, the temperature was kept at 35—40°. After the mixture had been stirred for 6 hr. and kept for a further 16 hr., *tert.*-butanol (*ca.* 400 c.c.) was distilled off under reduced pressure (internal temp., *ca.* 30°), and the residue diluted with water (1·5 l.). The solution was acidified (Congo-red) with hydrochloric acid, and the oily product extracted with ether (750 c.c.). The ethereal solution was washed with aqueous sodium hydrogen carbonate and dried ($MgSO_4$). After removal of the ether by distillation, the residue (138 g., 93%) set to a crystalline solid, which afforded the pure *ester*, m. p. 57—58° on crystallisation from ether at −70° (Found: C, 62·0; H, 7·4; N, 14·2. $C_{10}H_{14}O_2N_2$ requires C, 61·85; H, 7·2; N, 14·45%). Extensive decomposition occurred on attempted distillation of the substance under reduced pressure.

tert.-*Butyl αβ-Dicyano-α-methylbutyrate* (VI; R = Bu^t, R′ = Me).—*tert.*-Butyl cyanoacetate (105·8 g.) was condensed with acetaldehyde cyanohydrin (53·3 g.) as described above. After 16 hr., the solution was treated with methyl iodide (60 c.c.). The temperature rose spontaneously from 23° to 50°, and the reaction was completed by 1 hour's heating on the steam-bath. *tert.*-Butanol (*ca.* 500 c.c.) was then distilled off under reduced pressure, and the residue diluted with water (1 l.). The oily product was extracted with ether (450 c.c.), and the extract washed with N-sodium carbonate and dried ($MgSO_4$). After distillation of the ether, the residue was treated with a trace of potassium carbonate and distilled under reduced pressure (yield, 129 g., 83%; b. p. 92°/0·3 mm., n_D^{20} 1·4328) (Found: C, 63·1; H, 7·6; N, 13·5. $C_{11}H_{16}O_2N_2$ requires C, 63·45; H, 7·7; N, 13·45%).

tert.-*Butyl α-Benzyl-αβ-dicyanobutyrate* (VI; R = Bu^t, R′ = CH_2Ph).—*tert.*-Butyl cyanoacetate (70·5 g.) was condensed with acetaldehyde cyanohydrin (36 g.) in a solution of sodium (11·5 g.) in *tert.*-butanol (500 c.c.) as above. Benzyl chloride (72 c.c.) was then added, and the mixture boiled under reflux for 24 hr. After removal of most of the *tert.*-butanol under reduced pressure, the residue was diluted with water (625 c.c.), and the product extracted with ether (500 c.c.). The ethereal solution was dried ($MgSO_4$) and, after removal of the ether, the residue was distilled at 0·1 mm. (bath-temp. 140°) to remove excess of benzyl chloride. The residue (121 g., 85%) set to a pasty solid. Crystallisation from *tert.*-butanol afforded the pure *ester*, m. p. 96—97° (Found: C, 71·5; H, 6·7; N, 10·2. $C_{17}H_{20}O_2N_2$ requires C, 71·85; H, 7·05; N, 9·85%).

tert.-*Butyl αβ-Dicyano-β-phenylpropionate*.—A mixture of benzaldehyde (10·6 g.), *tert.*-butyl cyanoacetate (14·1 g.), and aqueous alcohol (30 c.c.; 60%) was treated with piperidine (35 drops). When the solution was shaken, the temperature rose spontaneously to 45°. The mixture was heated to 60°, cooled to 25°, and treated with water (10 c.c.). Sodium cyanide (4·9 g.) was added portionwise and with shaking during 10 min., the mixture being kept at 30—40°. After a further 0·5 hr., during which the mixture was occasionally shaken, a clear solution resulted. This was acidified (Congo-red) with hydrochloic acid, and the liquor decanted from the oily product, which soon solidified. The product was extracted with benzene (50 c.c.), the solution dried ($MgSO_4$), and the benzene distilled off under reduced pressure, giving a residue (22·9 g., 89%) which set to a pasty solid. Recrystallisation from benzene–ligroin or from *cyclo*hexane gave the pure *ester*, m. p. 80—81° (Found: C, 70·3; H, 6·2; N, 11·0. $C_{15}H_{16}O_2N_2$ requires C, 70·35; H, 6·25; N, 10·95%).

tert.-*Butyl αβ-Dicyano-α-methyl-β-phenylpropionate*.—*tert.*-Butyl αβ-dicyano-β-phenylpropionate (89 g.) in *tert.*-butanol (205 c.c.) was added to a solution of sodium (8·1 g.) in *tert.*-butanol (350 c.c.), at 25—30°. Methyl iodide (30 c.c.) was added; the temperature rose spontaneously from 25° to 40°. The mixture was boiled under reflux for 2 hr., after which most of the *tert.*-butanol was removed under reduced pressure. The residue was diluted with water (450 c.c.), and the product extracted with ether (450 c.c.). The extract was dried ($MgSO_4$), and the ether removed, giving a viscous oil (92·5 g.) which was not obtained pure. On attempted distillation under reduced pressure, it partly decomposed, giving α-methyl-β-phenylsuccinonitrile.

tert.-Butyl α-Cyano-α-methylacetoacetate (VIII).—Sodium *tert.*-butoxide, prepared by boiling sodium (8 g.) with *tert.*-butanol (350 c.c.) for 17 hr. and subsequently removing *tert.*-butanol by distillation under reduced pressure, was suspended in dry benzene (360 c.c.), and *tert.*-butyl α-cyanopropionate (53·5 g.) added. *tert.*-Butanol was removed as its azeotrope with benzene through a metal-packed column. The residual solution was cooled to 20° and acetyl chloride (50 c.c.) was added with stirring; the temperature rose spontaneously to 55°. The mixture was boiled under reflux for 1 hr., stored for 18 hr., and then shaken with water (500 c.c.) at 0°. The benzene solution was washed with N-sodium carbonate and dried ($MgSO_4$), and the benzene removed by distillation. Distillation of the residue under reduced pressure afforded *tert.-butyl α-cyano-α-methylacetoacetate* (41·5 g., 61%), b. p. 108—114°/20 mm., 55—60°/0·1 mm. (Found : C, 60·5; H, 7·7; N, 7·4. $C_{10}H_{15}O_3N$ requires C, 60·9; H, 7·6; N, 7·1%).

Preparation of Nitriles by Dealkylation and Decarboxylation of tert.*-Butyl Esters.*—(*a*) A mixture of the *tert.*-butyl ester and acetic acid (in some cases containing up to 5% of hydrogen chloride) was introduced dropwise into a vertical pyrolysis tube packed with pieces of silica and kept at 200—210° (internal thermocouple) by means of an electric-tube furnace. For small-scale work (*e.g.*, 0·05—0·1 mole), a pyrolysis tube measuring 12 × 2 cm. was suitable; on a larger scale, a tube of 20 × 3·5 cm. was preferred. Complete passage of the solution took 0·5—1·25 hr. according to the scale. The volatile products were collected in a receiver cooled in ethanol–solid carbon dioxide. The pyrolysis tube was purged with a small quantity of acetic acid and finally with nitrogen. The products were isolated and purified by fractional distillation under reduced pressure.

(*b*) The *tert.*-butyl ester was mixed with anhydrous toluene-*p*-sulphonic acid (4 g./mole) in a distillation flask attached to a condenser and receiver. The apparatus was evacuated by a water-pump, and the flask was heated by immersion in an oil-bath at 175—180°. The start of the reaction was marked by a considerable rise of pressure. After a few minutes, when evolution of gas had ceased, the pressure fell to 10—20 mm. and the product was distilled. The yields obtained by this method were usually inferior to those produced by method (*a*).

TABLE 4. *Preparation of nitriles by dealkylation and decarboxylation of* tert.*-butyl cyano-esters.*

tert.-Butyl ester pyrolysed	Wt. (g.)	Method	AcOH (c.c.)	HCl	Toluene-*p*-sulphonic acid (g.)	Product	Yield (%)
αβ-Dicyanobutyrate	23	*a*	12	+	—	Methylsuccinonitrile	12
,, ,,	19·4	*b*	—	—	0·4	,, ,,	14
αβ-Dicyano-α-methylbutyrate	20·8	*a*	5	—	—	αβ-Dimethylsuccinonitrile	81
,, ,,	20·8	*a*	5	+	—	,, ,,	74
,, ,,	20·8	*b*	—	—	0·4	,, ,,	62
α-Benzyl-αβ-dicyanobutyrate	52·8	*a*	55	—	—	α-Benzyl-β-methylsuccinonitrile	89
,, ,,	14·2	*a*	14·5	—	—	,, ,,	88
,, ,,	14·2	*a*	14·5	+	—	,, ,,	89
,, ,,	29·3	*b*	—	—	0·4	,, ,,	75
αβ-Dicyano-β-phenylpropionate	12·8	*b*	—	—	0·2	Phenylsuccinonitrile	45
αβ-Dicyano-α-methyl-β-phenylpropionate	43	*b*	—	—	0·65	α-Methyl-β-phenylsuccinonitrile	51
α-Acetyl-α-cyanopropionate	19·2	*a*	5	—	—	(Decomp. incomplete at 200—210°)	—
,, ,,	19·2	*a*	5	+	—	α-Acetylpropionitrile	88
		Temp. 220—230°					
,, ,,	30·3	*b*	—	—	0·6	,, ,,	64

+ Indicates that up to 5% of hydrogen chloride was added.

αβ-Dimethylsuccinonitrile, b. p. 122—135°/15 mm., obtained by any of the above methods, was a mixture of (±)- and *meso*-forms as pasty crystals. After being dried on a porous tile, the substance had m. p. 44—45° (Found : C, 66·5; H, 7·5; N, 26·0. Calc. for $C_6H_8N_2$: C, 66·65; H, 7·5; N, 25·95%). Crystallisation from ethanol–light petroleum afforded the (±)-form, m. p. 58°, described by Linstead and Whalley (*loc. cit.*). By method (*b*), a high-boiling product (b. p. 140°/0·3 mm.) was also obtained. This substance probably consisted of a mixture of stereoisomeric *α-cyano-αβ-dimethylsuccinimides* (Found : C, 55·0; H, 5·8;

N, 18·0. $C_7H_8O_2N_2$ requires C, 55·25; H, 5·3; N, 18·4%). Hydrolysis with hot, concentrated hydrochloric acid gave principally *meso*-αβ-dimethylsuccinic acid, m. p. 196° (Found : C, 49·1; H, 6·8%; equiv., 74. Calc. for $C_6H_{10}O_4$: C, 49·3; H, 6·85%; equiv., 73).

Methylsuccinonitrile was obtained in only small yield by pyrolysis of *tert.*-butyl αβ-dicyanobutyrate; the greater part of the product was a viscous oil, b. p. 130—140°/0·2 mm., believed to be a mixture of stereoisomeric α-cyano-β-methylsuccinimides. Both products gave methylsuccinic acid, m. p. 114°, on hydrolysis.

α-Benzyl-β-methylsuccinonitrile was obtained as a viscous oil, b. p. 122—132°/0·1 mm., consisting of a mixture of stereoisomers (Found : C, 78·4; H, 6·4; N, 14·8. $C_{12}H_{12}N_2$ requires C, 78·25, H, 6·5; N, 15·2%). On storage, the oil became semi-solid; the crystalline portion, after recrystallisation from benzene–ligroin, had m. p. 70°.

Phenylsuccinonitrile, after crystallisation from benzene–ligroin, had m. p. 67°, not depressed on admixture with an authentic sample. Mowry (*J. Amer. Chem. Soc.*, 1946, **68**, 2108) gives m. p. 68°. *α-Methyl-β-phenylsuccinonitrile* formed a viscous oil, b. p. 118—122°/0·3 mm., which partly crystallised (Found : C, 78·0; H, 6·4. $C_{11}H_{10}N_2$ requires C, 77·65; H, 5·9%). The crystalline portion had m. p. 80—81° after crystallisation from benzene–ligroin (Found : N, 16·95. $C_{11}H_{10}N_2$ requires N, 16·45%).

α-Acetylpropionitrile was isolated from the product of pyrolysis by dilution with water, neutralisation of the solution with sodium hydrogen carbonate, and extraction with ether. After being dried ($MgSO_4$), the extract was fractionally distilled, giving the keto-nitrile, b. p. 74—76°/15 mm., characterised as the semicarbazone, m. p. 162° (Found : C, 47·25; H, 6·8; N, 36·0. Calc. for $C_6H_{10}ON_4$: C, 46·75; H, 6·5; N, 36·35%); Mohr (*loc. cit.*) gives m. p. 153°.

Attempted Preparation of αβ-Dimethylsuccinonitrile by Other Methods.—From halogeno-compounds and metallic cyanides. Several attempts were made to prepare αβ-dimethylsuccinonitrile by heating 2 : 3-dichloro- or -dibromo-butane with metallic (sodium, cuprous, and mercuric) cyanides with and without solvents (2-methoxyethanol, aqueous ethanol, anhydrous pyridine, γ-picoline, and ethylene glycol). Products obtained included unchanged starting material, 3-bromobut-1-ene, other unsaturated compounds, and tar. No αβ-dimethylsuccinonitrile was obtained.

From αβ-unsaturated nitriles and hydrogen cyanide. (*a*) A mixture of angelonitrile and tiglonitrile gave a small yield of *meso*-αβ-dimethylsuccinic acid, m. p. 196°, when boiled with aqueous-alcoholic potassium cyanide for 24 hr.

(*b*) A mixture of angelonitrile and tiglonitrile (50 g.) was heated with anhydrous hydrogen cyanide (27 c.c.) and potassium cyanide (2 g.) in a steel bomb at 100—110° (bath temp.) for 72 hr. Fractional distillation of the product gave αβ-dimethylsuccinonitrile (2·1 g.; 3%), b. p. 125—135°/15 mm., which yielded on hydrolysis *meso*-αβ-dimethylsuccinic acid, m. p. and mixed m. p. 196°. When a mixture of angelonitrile and tiglonitrile (10 g.) was treated with hydrogen bromide and subsequently with water, a small yield of *β-bromo-α-methylbutyramide* was obtained. After crystallisation from benzene, this had m. p. 111—112° (Found : N, 7·9; Br, 44·0. $C_5H_{10}ONBr$ requires N, 7·8; Br, 44·45%).

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*Steric Hindrance in Analytical Chemistry. Part III.** 1-2′-*Pyridylisoquinoline and the Ferroin Reaction.*

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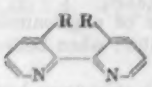
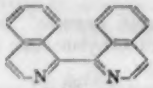
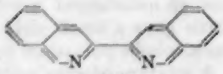
1-2′-Pyridyl*iso*quinoline has been synthesised. It gives a colour with traces of ferrous iron ($\lambda_{max.}$ 585 mμ; $\varepsilon_{max.}$ 11,500) confirming that the failure of this reaction with 1 : 1′-di*iso*quinolyl is due to steric hindrance. 3 : 4-Dihydro-1-2′-pyridyl*iso*quinoline gives a stronger coloured complex ($\lambda_{max.}$ 586 mμ; $\varepsilon_{max.}$ 15,600).

The formation of an intensely red, water-soluble complex between ferrous iron and 1 : 10-phenanthroline forms the basis of the well-known "ferroin" reaction which is also given by 2 : 2′-dipyridyl (I; R = H) and many compounds related to it by substitution or annelation. The reaction even functions with certain aza-derivatives such as 7-ethoxycarbonyl-8-hydroxy-1-methyl-3 : 4 : 5-triazaphenanthrene and 4-*p*-methoxyphenyl-3-2′-pyridylcinnoline (Irving and Williams, *Analyst*, 1952, **77**, 813). From a review of published data and a study of new compounds (Irving and Mellor, to be published) it is clear that the essential condition for the ferroin reaction is the specific grouping –N=C–C=N– forming part of an aromatic system, and capable of forming a five-membered chelate ring. However substituents (or rings) adjacent to the nitrogen atoms can cause steric hindrance to co-ordination and partly, or completely inhibit the reaction with ferrous ions (cf. Irving, Cabell, and Mellor, *J.*, 1953, 3417).

Case (*J. Org. Chem.*, 1952, **17**, 471) reports that the di*iso*quinolyl (III) gives an orange colour with ferrous iron while the ferroin reaction fails completely with (II), although this


(I)


(II)


(III)

compound has no substituents adjacent to the nitrogen atoms This latter observation is not surprising for, in addition to the frontal or "packing" effect, the intensity of the ferroin reaction is reduced to a greater or less extent by substituents remote from the co-ordinating nitrogen atoms if, through steric hindrance, they tend to prevent the coplanarity of the heterocyclic rings with the five-membered ring formed by co-ordination to metal. Fig. 1 represents the plane of a chelated molecule of the dipyridyl (I) based on conventional van der Waals radii and interatomic distances. The "interference envelopes" shown by broken lines demonstrate the degree of steric hindrance between a 3-methyl and a 3′-hydrogen atom, and the considerably greater interference between a 3-methyl and a 3′-methyl group. In accordance with the predictable loss of resonance energy it is found (Cagle and Smith, *J. Amer. Chem. Soc.*, 1947, **69**, 1860) that 3 : 3′-dimethyl-2 : 2′-dipyridyl gives a weaker coloured ferrous complex ($\varepsilon_{max.}$ = 1770) than the parent dipyridyl ($\varepsilon_{max.}$ = 8650) although the wave-length of maximum absorption remains almost unchanged. Many other examples of this "coplanarity effect" are known among reagents which undergo the "cuproin" reaction (Irving and Mellor, to be published).

The failure of the di*iso*quinolyl (II) to exhibit the ferroin reaction is doubtless due to the strong interference between the 8 and the 8′ position where, as may be inferred from Fig. 2, the hydrogen atoms would completely overlap if the molecule were coplanar. To test this point we have synthesised 1-2′-pyridyl*iso*quinoline (V) where, as shown in Fig. 2, steric hindrance is limited to interference between the more remote 8 and 3′ position and should be less than that operating in 3 : 3′-dimethyl-2 : 2′-dipyridyl (cf. Fig. 1).

2-Phenyl-*N*-picolinoylethylamine (conveniently prepared from methyl picolinate and 2-phenylethylamine) was cyclised to 3 : 4-dihydro-1-2′-pyridyl*iso*quinoline (IV) by Dekker

* Part II. *J.*, 1953, 3417.

and Kropp's modification (*Ber.*, 1909, **42**, 2075) of the Bischler–Napieralski reaction. This dihydro-base was not oxidised by hot acid permanganate under the conditions used by Pictet and Kay (*ibid.*, 1909, **42**, 1973) to dehydrogenate 3 : 4-dihydro-1-phenyl*iso*quinoline, but catalytic dehydrogenation to the desired 1-2′-pyridyl*iso*quinoline (V) was effected with palladium black in a modification of the procedure used by Hey and Williams (*J.*, 1951, 1527) to prepare 1-3′-pyridyl*iso*quinoline.

After this paper had been submitted we learnt that the base (V) had been synthesised independently by the direct action of pyridyl-lithium upon *iso*quinoline (Knott and Breckenridge, *Canad. J. Chem.*, 1954, **32**, 512). This synthesis is not unequivocal, but the possibility of substitution's having occurred in the 4-position of the *iso*quinoline system

FIG. 1.

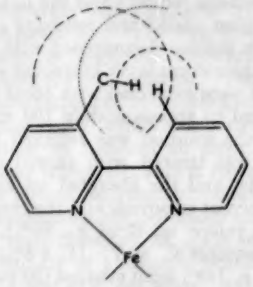
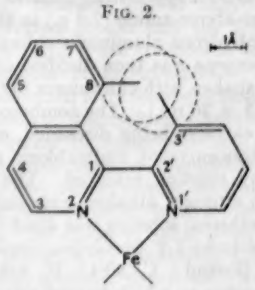
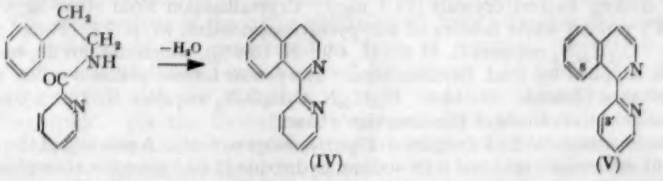


FIG. 2.



appeared unlikely from the close similarity between the spectrum of the pyridyl*iso*quinoline and that of compounds prepared from 4-methyl-quinolines by treatment with pyridyl-lithium. Identity with our preparation of 1-2′-pyridyl*iso*quinoline (V), whose structure is unambiguously determined by synthesis, was first established by the comparison of absorption spectra of the base and its ferrous complex, and confirmed by mixed melting-point determinations on a specimen of the base (and its picrate) kindly made available by Professor Breckenridge.



With traces of ferrous iron in a buffer of pH 5—6 containing hydroxylamine, 1-2′-pyridyl*iso*quinoline gave a clear reddish-blue colour which was stable for some days. The absorption spectrum showed a single broad band in the visible region with $\lambda_{max.} = 585$ mμ; $\varepsilon_{max.} = 11{,}500$; $\lambda_{min.} = 430$ mμ; $\varepsilon_{min.} = 1{,}100$. The ferroin reaction with this reagent is thus considerably more delicate than with 2 : 2′-dipyridyl ($\varepsilon_{max.} = 8650$) and comparable with that of 1 : 10-phenanthroline ($\varepsilon_{max.} = 11{,}100$). 1-2′-Pyridyl*iso*quinoline also gave a brown cuprous complex extractable into *iso*amyl alcohol. Its spectrum consisted of two broad overlapping bands causing general absorption from 475 to 575 mμ ($\varepsilon \sim 3{,}300$) and was very similar to that of the cuprous complex of the analogous 1-2′-quinolyl*iso*quinoline (λ 450—550 mμ; $\varepsilon \sim 2{,}550$) reported by Hoste (*Analyt. Chim. Acta*, 1950, **4**, 23).

3 : 4-Dihydro-1-2′-pyridyl*iso*quinoline (IV) also formed a ferrous complex which did not fade during several days. The spectrum closely resembled that of the base (V) since $\lambda_{max.} = 586$ mμ but the intensity of absorption was much greater ($\varepsilon_{max.} = 15{,}600$). Ferric ions gave a very pale yellow colour, and cuprous ions gave a brownish yellow precipitate at pH 6 which dissolved in amyl alcohol to give a brown solution which faded rapidly.

That the ferroin reaction should be more sensitive with the dihydro-base (IV) than with 1-2′-pyridyl*iso*quinoline (V) was unexpected : presumably the increase in conjugation and

aromaticity on dehydrogenation is more than offset by the increased steric hindrance due to the less flexible *iso*quinoline ring.

Experimental

2-Phenyl-N-picolinoylethylamine.—Methyl picolinate (6·75 g.; Engler, *Ber.*, 1894, **27**, 1784) and 2-phenylethylamine (9 ml.) were boiled for 30 min., methanol (1 ml.) being collected through a 50-cm. Vigreux column. The mixture was refluxed for a further 12 hr. and then heated at 80—100°/4 mm. to remove excess of phenylethylamine. Distillation of the residue gave an oil (10·3 g., 92%), b. p. 156—158°/4 mm., which on cooling formed crystals of *2-phenyl-N-picolinoylethylamine*. The compound crystallised from light petroleum (b. p. 40—50°; 25 parts) as white needles, m. p. 36° (Found: C, 74·5; H, 6·2. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2%).

3 : 4-Dihydro-1-2′-pyridylisoquinoline.—Phosphorus pentachloride (9 g.) was added to a solution of the above amide (7·8 g.) in thiophen-free benzene (80 ml.) and the mixture refluxed for 1 hr. Anhydrous aluminium chloride (9 g.) was then added and refluxing continued for 3 hr.; the benzene was then distilled off and the dark residue decomposed with water. The mixture was shaken with chloroform (50 ml.) and the chloroform layer extracted with N-hydrochloric acid (3 × 20 ml.). The combined acid extracts were extracted with ether (2 × 30 ml.), the ethereal extracts being discarded, and concentrated to approximately 100 ml. After the addition of concentrated hydrochloric acid (50 ml.) the solution was refluxed for 17 hr. to hydrolyse any starting material. The hot solution was treated with animal charcoal, the filtrate made strongly alkaline with sodium hydroxide, and the liberated oil extracted with ether. The ethereal solution was dried (K_2CO_3), the solvent removed, and the residue distilled, giving *3 : 4-dihydro-1-2′-pyridylisoquinoline* as a pale yellow oil (2·91 g., 39%), b. p. 142—143°/4 mm. (Found: C, 80·4; H, 6·0. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8%). This base yielded a *monopicrate* which formed yellow needles, m. p. 149°, from ethanol (50 parts) (Found: C, 54·6; H, 3·5; N, 16·2. $C_{14}H_{12}N_2,C_6H_3O_7N_3$ requires C, 54·9; H, 3·5; N, 16·0%). The *perchlorate* formed white needles, m. p. 212° (decomp.), from acetic acid (10 parts) (Found: C, 54·4; H, 3·6; N, 9·1. $C_{14}H_{12}N_2,HClO_4$ requires C, 54·5; H, 4·2; N, 9·1%).

1-2′-Pyridylisoquinoline.—3 : 4-Dihydro-1-2′-pyridylisoquinoline (29·0 mg.) and palladium black (30·0 mg.; prepared according to Willstätter, *Ber.*, 1921, **54**, 113) were heated for 2 hr. at 240—245° in a 1-ml. bulb attached to a length of glass tubing. After liquid condensate had been washed back into the bulb with acetone and the solvent distilled off, heating was continued at 265—270° for 1½ hr. The mixture was distilled at 130—135°/0·2 mm. (air-bath) giving an oil which on cooling formed crystals (19·7 mg.). Crystallisation from ether–light petroleum (b. p. 60—75°) yielded white needles of *1-2′-pyridylisoquinoline*, m. p. 72° (Found: 81·6; H, 4·8; N, 13·5. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·6%), which did not depress the m. p. of a specimen supplied by Prof. Breckenridge. The *picrate* formed yellow needles, m. p. 166—167°, from ethanol (Found: N, 15·9. $C_{14}H_{10}N_2,C_6H_2O_7N_3$ requires N, 16·1%) and did not depress the m. p. of the picrate of Breckenridge's base.

Absorption Spectra.—(a) *3 : 4-Dihydro-1-2′-pyridylisoquinoline.* A solution of the perchlorate in a mixture of ethanol (95 ml.) and 0·1N-sodium hydroxide (5 ml.) gave the absorption spectrum of the free base. This was a single band with $\lambda_{max.}$ = 265 mμ, $\varepsilon_{max.}$ = 11,100; $\lambda_{min.}$ = 240 mμ, $\varepsilon_{min.}$ = 7,800. In 0·05N-hydrochloric acid there was a bathochromic shift to $\lambda_{max.}$ = 290 mμ, $\varepsilon_{max.}$ = 14,100; $\lambda_{min.}$ = 245 mμ, $\varepsilon_{min.}$ = 4,460. Solutions of the ferrous complex (8×10^{-5}M in an acetate buffer of pH 4·9 containing hydroxylamine) showed $\lambda_{max.}$ = 586 mμ, and $\varepsilon_{max.}$ = 15,600. Beer's law was obeyed up to at least 25 p.p.m. of iron.

(b) *1-2′-Pyridylisoquinoline.* The free base in 95% ethanol gave a simple band spectrum with $\lambda_{max.}$ = 221 mμ, $\varepsilon_{max.}$ 41,800, and $\lambda_{max.}$ = 320 mμ, $\varepsilon_{max.}$ = 6,600. In acid solution there was a bathochromic shift to $\lambda_{max.}$ = 231 mμ, $\varepsilon_{max.}$ = 33,700 in 0·1N-hydrochloric acid, and $\lambda_{max.}$ = 239 mμ, $\varepsilon_{max.}$ = 31,000 in 2·5M-hydrochloric acid. An isosbestic point at 235 mμ suggests that a second proton is being co-ordinated in the more acid solutions. The absorption spectra of the ferrous and cuprous complexes are reported above.

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Fluorosulphonic Acid. Part II. Ionization in the Anhydrous Solvent and the Formation of Complex Fluorides.*

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[Reprint Order No. 5665.]

The preparation of complex fluorides, by means of solvents, between component fluorides close together in the periodic classification is discussed. Fluorosulphonic acid is considered as a possible solvent. Its main self-ionization, which gives rise to a conductivity between that of anhydrous hydrofluoric and sulphuric acids, is to a solvated proton and the fluorosulphonate ion. The ions HSO_3^+, H_2F^+, and $S_2O_6F^-$ are considered to be present in negligible amounts. Fluorides soluble in fluorosulphonic acid enhance the conductivity. The alkali fluorides, which form fluorosulphonates by elimination of hydrogen fluoride, are the bases in this system. Antimony pentafluoride, which contains an antimony anion in fluorosulphonic acid solution, is believed to form hexafluoroantimonic acid by elimination of sulphur trioxide. This is regarded as an acid and indeed can be neutralized with potassium fluorosulphonate solution to give a conductometric minimum at approximately equimolecular proportions. Solutions of other fluorides are then classified as acids or bases with reference to potassium fluorosulphonate or antimony pentafluoride in conductometric titrations. AuF_3, TaF_5, and PtF_4 are acids: AsF_3, SbF_3, BrF_3, and IF_5 are bases. The proton acid $HClO_4$ appears not to behave as an acid in the fluorosulphonic acid system. Organic compounds can function as bases, and both pyridine and nitrobenzene have been titrated with antimony pentafluoride.

The limitations imposed by solvents in the preparation of complex fluorides have been mentioned in Part I *. When the component fluorides are widely separated in the periodic classification the practical limits to preparation of solvent-free complexes are imposed by sparing solubilities of fluorides, and further reaction with the solvent after solution. The most serious of the latter effects, apart from solvation of cation or anion, is solvolysis, a reversal of the neutralization type of reaction. Solvolysis in bromine trifluoride is typical and has been discussed by Sharpe (*J.*, 1950, 2907, 3444). It is intimately connected with the difference in acid and base strengths as well as their absolute magnitude. (In the formation of complex fluorides it is considered that the component fluorides react with the solvent to form acids or bases which contain cations or anions, respectively, characteristic of the solvent. The acids are neutralized by bases to give the complexes. In fluoride solvents an alternative description of the initial process is that the acid is a fluoride-ion acceptor, the base a fluoride donor. It is in these senses that the terms acid and base are used.) The way to eliminate solvolysis is therefore by adjustment of acid and base strengths and this is only possible if a sufficient range of solvents or solvent mixtures is available.

When the component fluorides are close in the periodic classification the difficulties are accentuated on account of the smaller difference in properties between the acid and base components. The high electronegativity of fluorine, however, should permit the closest approach for any of the halides or pseudo-halides. This would occur between halides in the same group or even between halides of the same element in different valency states. The preparation of double fluorides of group V elements is of interest for valency theory, and serves to demonstrate the difficulties. With bromine trifluoride only the pentafluorides can form solutions, and these behave as acids. When pairs of fluorides are mixed, only the corresponding pairs of acids can be isolated. A solvent is required which is not oxidising and has an acid strength between the strengths of the fluoride components of a complex. One possibility is to use a fluoride of group V itself as the solvent.

* Part I, *J.*, 1954, 2840.

Arsenic trifluoride has been used to prepare an approximately equimolar compound of antimony tri- and penta-fluorides, the missing member of the series prepared by Ruff and Plato (*Ber.*, 1904, **37**, 673). The uses of antimony trifluoride and selenium tetrafluoride as solvents are obvious extensions. However, it is doubtful whether these solvents will have any general application and it is for this reason that fluorosulphonic acid has been studied.

Little is known of its solvent or acid properties. In Part I (*loc. cit.*) it was shown to differ from sulphuric acid in being a true compound and not a constant-boiling mixture, and in dilute aqueous solution it ionizes to hydroxonium and fluorosulphonate ions. The anhydrous acid has a conductivity of $2{\cdot}20 \times 10^{-4}$ mho at 25°, intermediate between those of sulphuric and hydrofluoric acids. (Gillespie and Wasif, *J.*, 1953, 203, give $1{\cdot}03 \times 10^{-2}$ at 25° for sulphuric acid; Fredenhagen and Cadenbach, *Z. anorg. Chem.*, 1928, **178**, 289, give $1{\cdot}4 \times 10^{-5}$ at −15° for hydrogen fluoride.) The conductivity varies exponentially with temperature between −78° and 58°, and in common with certain other fluorides the ratio of the activation energies of viscous flow and conduction is less than unity (Fairbrother, Frith, and Woolf, *J.*, 1954, 1031). The conductivity can be explained by self dissociation but a choice of equilibria, which may not be mutually exclusive, is possible. For simplicity the unsolvated fluoride and hydrogen ions are given in the following schemes instead of the more likely $HSO_3F_2^-$ and $H_2SO_3F^+$ ions:

$$HSO_3F \rightleftharpoons H^+ + SO_3F^- \quad . . . . . (1)$$

$$HSO_3F \rightleftharpoons HSO_3^+ + F^- \quad . . . . . (2)$$

$$2HSO_3F \rightleftharpoons H_2F^+ + S_2O_6F^- \quad . . . . . (3)$$

The evidence shows that the first ionization is the predominant one. The only gas produced on electrolysis of the anhydrous acid is hydrogen at the cathode. In the initial stages 0·5 mole of gas is liberated for each Faraday of electricity. This is compatible with (1) or (3) but not (2), since the fluoride ion would need to discharge as fluorine. The transport of fluorine to the anode renders (3) improbable, since the relative mobility of the ions would tend to transport it in the opposite direction. In favour of (1) are the facts that (i) the molecular conductivity of potassium fluorosulphonate solutions is practically independent of dilution when the solvent conductivity is deducted; (ii) the solvent becomes oxidising at the anode during electrolysis and, for example, tervalent is converted into quinquevalent antimony. The former (i) is analogous to the behaviour of bisulphates in anhydrous sulphuric acid (Hantzsch, *Z. phys. Chem.*, 1907, **61**, 257) and a similar repression of solvent ionization, by the fluorosulphonate ion of the salt, is indicated. The latter (ii) is in accord with the formation of an oxidising perdifluorosulphonate ion: $2SO_3F^- - e^- \longrightarrow S_2O_6F_2$. The other ionizations may occur to a minor extent. The presence of HSO_3^+ would explain the sulphonation of benzene (Meyer and Schramm, *Z. anorg. Chem.*, 1932, **206**, 24) and such an ion has been postulated to explain sulphonations in oleum (Brand and Horning, *J.*, 1952, 3922). The existence of the ions of equilibrium (3) is less certain. The $S_2O_6F^-$ ion has been reported only recently in an unstable potassium salt formed from sulphur trioxide and potassium fluorosulphonate (Lehmann and Kolditz, *ibid.*, 1953, **272**, 69), but there is no evidence from conductivity data of a second acid in the HF–SO_3 system. The conductivity decreases steadily from a maximum at HF,SO_3 through the composition $HF,2SO_3$.

The evidence for the H_2F^+ ion was based on the work of Hantzsch (*Ber.*, 1930, **63**, 1789) who claimed to have prepared the crystalline tetrafluoroborate and perchlorate by mixing hydrogen fluoride with boron fluoride and perchloric acid respectively. These compounds were solids whose m. p.s were well above those of the components. By analogy with his previous work on nitric acid–perchloric acid mixtures he assigned them ionic structures. His results have been controverted in recent years, for the compound $H_2NO_3^+ClO_4^-$ appears to have been a mixture of nitronium and hydroxonium perchlorates contaminated with nitric acid (Goddard, Hughes, and Ingold, *J.*, 1950, 2559), and $H_2F^+ClO_4^-$ appears equally fictitious, since Brauer and Distler (*Z. anorg. Chem.*, 1954, **275**, 157) failed to isolate any appreciable solid, apart from traces of hydroxonium perchlorate due to unavoidable moisture, when hydrogen fluoride was mixed with perchloric acid. The entity of the

compound $H_2F^+BF_4^-$ is disproved by the observations of McCauley and Lien (*J. Amer. Chem. Soc.*, 1951, **73**, 2013) who showed that there was no appreciable interaction of boron trifluoride and hydrogen fluoride except in the presence of basic hydrocarbons. Lange disputed the ionization $HSO_3F + H_2SO_4 \rightleftharpoons H_2F^+ + HS_2O_7^-$ because no pyrosulphate ions can be detected (Simons, "Fluorine Chemistry," Academic Press Inc., N.Y., 1950, Vol. I, p. 169). Finally, the boron trifluoride dihydrate, once formulated as $H_2F^+BF_2(OH)_2^-$ (Sowa, Kroeger, and Nieuwland, *J. Amer. Chem. Soc.*, 1935, **57**, 454) by analogy with Hantzsch's $H_2F^+BF_4^-$, has been shown by electrolytic transport in the melt and by conductivity data in solution, to be $H_3O^+BF_3{\cdot}OH^-$ (Greenwood and Martin, *J.*, 1951, 1915; Wamser, *J. Amer. Chem. Soc.*, 1951, **73**, 409). Although there is no longer any evidence for the existence of H_2F^+ in the solid state or in aqueous solution, there is some evidence, from the formation of complex fluorides by neutralization reactions in hydrogen fluoride (Woolf, *J.*, 1950, 3678) and from transport experiments in fluorosulphonic acid, for the existence of equilibrium amounts of this ion. Hydrogen fluoride is readily soluble in fluorosulphonic acid, more than an equimolecular amount being absorbed without evolution of much heat. The solutions, which contain free hydrogen fluoride as indicated by their high vapour tension and attack on silicate glass, are completely separable on distillation. Electrolysis, which causes a net transport of fluorine to the cathode compared with anodic transport of the solvent, shows a positive ion containing the elements. However, it is concluded that the amount of ionization of fluorosulphonic acid to H_2F^+, HSO_3^+, or $S_2O_6F^-$ can only be minute.

The behaviour of proton acids in fluorosulphonic acid depends primarily on their acid strength. There can be few acids able to donate protons to fluorosulphonic acid if it is as strong as indicated in aqueous solution (Part I). Sulphuric acid may be such an acid but the multiplicity of possibilities hampers interpretation ($H_2SO_4 + HSO_3F \rightleftharpoons H_2SO_3F^+ + HSO_4^-$ or $H_3O^+ + S_2O_6F^-$ or $H_2F^+ + HS_2O_7^-$ or $H_3SO_4^+ + SO_3F^-$). It has been shown that sulphuric acid forms solutions about as conducting as those of potassium fluorosulphate but for which the molecular conductivity varies with dilution. Perchloric acid has also been examined briefly and the results described below indicate that its proton is not donated to fluorosulphonic acid.

Fluorides can be qualitatively divided into three groups according to their solubility in fluorosulphonic acid: *viz.*, soluble, KF, AgF, AuF_3, AsF_3, SbF_5, TaF_5, BrF_3, and IF_5; sparingly soluble, BF_3, SnF_4, SbF_3, and PtF_4; and insoluble, BiF_3 and TlF_3. The soluble or sparingly soluble fluorides enhance the conductivity of fluorosulphonic acid. The alkali fluorides dissolve with evolution of heat, elimination of hydrogen fluoride, and formation of fluorosulphonates (Traube, Horenz, and Wunderlich, *Ber.*, 1919, **52**, 1272). Potassium fluorosulphonate is a strong electrolyte in fluorosulphonic acid, the molecular conductivity of these solutions (*ca.* 240) being about double the values attained in the less viscous solvents, bromine trifluoride and water. Thus the ions have an abnormal mobility in fluorosulphonic acid and there is a similarity with solutions of bisulphates in sulphuric acid and alkali fluorides in hydrogen fluoride. It is probable that the abnormal mobility of the fluorosulphonate ion results from a charge transfer of the Grotthus chain type. The metal fluorosulphonates are bases in the fluorosulphonic acid solvent system.

Antimony pentafluoride is readily soluble in fluorosulphonic acid without any evolution of hydrogen fluoride. Its molecular conductivity, corrected for solvent conductivity, varies with dilution. At infinite dilution it is about half that of potassium fluorosulphonate. The antimony is present as an anion because electrolysis of its solution transports antimony to the anode. When antimony pentahalides are dissolved in other solvents (ICl, $AsCl_3$, $POCl_3$, $SOCl_2$, CNCl, HF, AsF_3, BrF_3, IF_5), the antimony is invariably found in complex anions.

If the self-ionization of fluorosulphonic acid to H^+ and SO_3F^- is accepted, there are only two reasonable ionizations for antimony pentafluoride

$$SbF_5 + HSO_3F \rightleftharpoons H^+ + SbF_5SO_3F^- \quad \text{or} \quad H^+ + SbF_6^- + SO_3$$

The latter is preferred because abnormal co-ordinations are required in the first alternative: the ion $SbF_5SO_3F^-$ would require five-fold co-ordination of sulphur, and $SbF_6SO_3^-$ would

require seven-fold co-ordination of antimony, but neither type of co-ordination has been previously encountered. The presence of free sulphur trioxide is compatible with the lower conductivity of antimony pentafluoride solutions than of potassium fluorosulphonate solutions. The decrease of solvent conductivity on addition of sulphur trioxide has been mentioned previously. It is recognized that the choice of ionizations is somewhat arbitrary, but the experimental results are most readily explained if potassium fluoride and antimony pentafluoride form a base and an acid by respective displacement of hydrogen fluoride and sulphur trioxide from the solvent.

Neutralization of antimony pentafluoride solution with potassium fluoride solution has been followed conductometrically. The conductivity of an antimony pentafluoride solution falls sharply on the initial additions of the more conducting potassium fluorosulphonate solution, and rises only after the addition of about an equimolar amount of the fluorosulphonate. An excellent end-point is obtained with pyridinium fluorosulphonate, and this salt has been titrated in the reverse manner by addition of the pentafluoride. A cusp-like conductivity curve yields an end-point close to equimolecular proportions. Nitrobenzene forms a yellow solution in fluorosulphonic acid which also produces a sharp end-point when titrated with antimony pentafluoride. The pyridine and nitrobenzene bases have approximately the same molecular conductivities as potassium fluorosulphonate. (The approximate values without solvent correction are 239 at a concentration of 0·080 mole/1000 g. of solvent, 230 at 0·049 and 248 at 0·044, respectively.) This is analogous to the behaviour of bisulphates in sulphuric acid and illustrates again the abnormal mobility of the fluorosulphonate ion. These titrations can all be represented as neutralization reactions of the type $R^+SO_3F^- + H^+SbF_6^- \longrightarrow R^+SbF_6^- + HSO_3F$. The cation formed from nitrobenzene, $C_6H_5{\cdot}NO_2H^+$, has been found in sulphuric acid solutions where its identity has been established by cryoscopic and spectrometric measurements (Gillespie, *J.*, 1950, 2542; Brand, Horning, and Thornley, *ibid.*, pp. 997, 1374).

Other fluorides can be classified as acids or bases by examination of their behaviour with potassium fluorosulphonate or antimony pentafluoride in conductometric titrations, together with transport studies. Auric fluoride is readily soluble in fluorosulphonic acid, the solution having a yellow-orange colour like that of aqueous solutions of chloroauric acid. On titration with antimony pentafluoride the conductivity of the solution increases steadily without any inflection on the curve. With potassium fluorosulphonate, however, there is a definite minimum in the curve, the shape of which resembles the titration curve of antimonic fluoride with potassium fluorosulphonate. An electrolysis experiment, in which gold is deposited cathodically, appears to contradict the conclusion that auric fluoride is an acid, but it is not unusual for solutions of complex gold anions to deposit gold at cathodes (see Woolf, *J.*, 1954, 252). There is a possibility of amphoteric behaviour, since auric fluoride combines with sulphur trioxide. The compound isolated, $AuF_3{,}2{\cdot}7SO_3$, could be a mixture of fluorosulphonates but it is unsound to regard all compounds of fluorides with sulphur trioxide as fluorosulphonates.

In group III the extreme members boron and thallium trifluoride have been examined. The latter is insoluble, and the former about as soluble as in sulphuric acid or hydrocarbons (*ca.* 46 ml./g. at 15°). It is eliminated completely on being heated and presumably dissolves without reaction in the solvent. It seems that boron trifluoride is unable to displace sulphur trioxide from fluorosulphonic acid since even in the presence of potassium fluorosulphonate no tetrafluoroborate is formed. Stannic fluoride was too sparingly soluble (*ca.* 0·2 g./100 ml.) for any reliable conductometric titrations to be made.

In group V the most soluble trifluoride is that of arsenic. Antimony trifluoride is sparingly soluble, and bismuth trifluoride insoluble. Arsenic trifluoride gives a conductivity minimum with antimony pentafluoride but not with potassium fluorosulphonate, in contrast to tantalum pentafluoride which gives no inflection with antimony pentafluoride but transports tantalum to the anode on electrolysis. Antimony trifluoride also gives a minimum in the conductivity curve with the pentafluoride. Electrolysis of the solution shows a net transport of antimony to the cathode, although the electrolysis is complicated by oxidation of Sb^{III} to Sb^{V} and reduction to Sb^0 at anode and cathode respectively. Thus the trifluorides of Group V behave as bases and the pentafluorides as

acids in fluorosulphonic acid solutions. Interaction is possible between pairs of elements in different valency states.

The fluorides of group VI, which are under investigation by Robinson and his co-workers, have not been examined, but it appears likely that the quadrivalent fluorides will behave as bases. A compound SeF_4,SO_3 has already been formulated as SeF_3,SO_3F (Aynsley, Peacock, and Robinson, *J.*, 1952, 1231; Peacock, *J.*, 1953, **3617**). The sexavalent fluorides, which form complexes with alkali fluorides under pressure (Martin, Albers, and Dust, *Z. anorg. Chem.*, 1951, **265**, 128), may react with tetrafluorides in fluorosulphonic acid solutions.

In group VII, bromine trifluoride and iodine pentafluoride react as bases since they can be titrated with antimonic fluoride but not potassium fluorosulphonate solutions. The bromine in bromine trifluoride solutions is transported in a cation. The behaviour of iodine pentafluoride as a base may explain a previous failure to prepare potassium hexafluoroiodate from potassium fluoride and iodine pentafluoride in hydrogen fluoride (*J.*, 1950, 3678). Iodine pentafluoride may form the base $IF_4^+HF_2^-$ rather than the acid $H^+IF_6^-$ in hydrogen fluoride solution. Rogers and Katz (*J. Amer. Chem. Soc.*, 1952, **74**, 1375) also postulate that bromine and iodine fluorides are basic in hydrogen fluoride. Rogers (personal communication) points out that the factor which may decide the mode of ionization is the large energy of ionization of hydrogen fluoride.

The only group VIII fluoride examined has been platinic fluoride which is sparingly soluble. An approximate titration shows that it is acidic with potassium fluorosulphonate.

In many of the titrations described, the end-points were nearer 2 : 1 or 3 : 1 proportions rather than 1 : 1. The simplest explanation in the case of bases is the formation of di- or tri-nuclear cations. For example, antimony pentafluoride was found equivalent to two molecules of the trifluoride so that the postulated reactions would be

$$2SbF_5 + HSO_3F \rightleftharpoons (Sb_2F_9)^+SO_3F^- + HF$$

and

$$SbF_5 + HSO_3F \rightleftharpoons H^+SbF_6^- + SO_3$$

followed by

$$(Sb_2F_9)^+SO_3F^- + H^+SbF_6^- \longrightarrow (Sb_2F_9)^+SbF_6^- + HSO_3F$$

Ruff and Plato's compound $SbF_5,2SbF_3$ (*loc. cit.*) may have this ionic structure, and the possibility of a polycation is strengthened by the existence of analogous polyanions in $CsSb_2F_7$ and $NaSb_4F_{13}$. The low molecular conductivity of antimony trifluoride, about a fifth of that of fluorosulphonates, shows that it is incompletely ionized as a fluorosulphonate. Another explanation may be that these fluorides react further with the solvent. That some reaction does occur is shown by a decrease in conductivity with time, of, *e.g.*, bromine trifluoride solutions. The formation of $S_2O_5F_2$ and $S_3O_8F_2$ which occurs under more drastic conditions with fluorides and sulphur trioxide (Hayek and Koller, *Monatsh.*, 1951, **82**, 940; Schmidt, *ibid.*, 1954, **85**, 452; Lehmann and Kolditz, *Z. anorg. Chem.*, 1953, **272**, 73) may occur to some extent with fluorides in fluorosulphonic acid. The di- and tri-sulphuryl fluorides would not be expected to ionize appreciably in fluorosulphonic acid, just as sulphuryl chloride is non-ionized in sulphuric acid. Further investigation will be required to elucidate these problems but our main thesis, that fluorides are separable into two divisions according to whether they titrate as acids or bases, is unaffected.

Perchloric acid solutions (see p. 442) resemble fluorosulphonates in that they can be titrated with antimony pentafluoride but not potassium fluorosulphonate. This leads to the unexpected conclusion that perchloric acid is a proton acceptor in fluorosulphonic acid. However, the presence of chlorine in a positive oxy-ion has been demonstrated recently by the preparation of the complex fluorides, $ClO_2^+BF_4^-$ and $ClO_2^+SbF_6^-$ (Schmeisser and Ebenhoech, *Angew. Chem.*, 1954, **66**, 230; Woolf, *J.*, 1954,) so that the existence of a septavalent chlorine oxy-cation is more acceptable. The ionization could be of the type $2HSO_3F + HClO_4 \rightleftharpoons ClO_3^- + H_3O^+ + 2SO_3F^-$. Examination of solutions of chloryl fluoride and nitryl fluoride in fluorosulphonic acid, which should react as bases, may throw some light on the nature of perchloric acid solutions.

Fluorosulphonic acid has been used to prepare simple fluorides and fluorosulphonates from oxides and halides (Engelbrecht and Grosse, *J. Amer. Chem. Soc.*, 1954, **76**, 2042;

Hayek, Puschmann, and Czaloun, *Monatsh.*, 1954, **85**, 359). The above work indicates that fluorosulphonic acid can also be applied to the preparation of complex fluorides by means of neutralization reactions. It would be premature, however, to attempt the latter without a clearer understanding of ionization in fluorosulphonic acid, and it is suggested that spectrometric and ebullioscopic techniques might be profitably employed with non-reactive solutes.

Experimental

Attempted Preparation of Group V Double Fluorides with Bromine Trifluoride.—The following pairs of fluorides were mixed (in practice the elements or oxides used were converted into fluorides by the solvent): SbF_5–AsF_5, SbF_5–PF_5, AsF_5–VF_5, and SbF_5–TaF_5. The respective products were SbF_5,BrF_3, SbF_5,BrF_3, no residue, and mixture of SbF_5,BrF_3 and TaF_5,BrF_3. These mixtures cover all combinations of volatile and non-volatile acids. In all cases the products were those which would result if the fluorides reacted separately with the solvent.

Reactions in Arsenic Trifluoride (*J.*, 1950, 2200).—Antimony trifluoride (0·5 g.) was refluxed for an hour with arsenic trifluoride. The bulk of the solvent was removed by distillation at atmospheric pressure, the rest *in vacuo*, and the residue analysed (Found: F, 38·3; As, 24·4%; equiv., 314. SbF_5,AsF_3 requires F, 36·7; As, 24·1%; equiv., 311).

Antimony tri- and penta-fluoride were mixed in equimolar amounts in arsenic trifluoride and heated for a short time, and excess of solvent removed as above. The residue was found to be $SbF_3,0{\cdot}98SbF_5,0{\cdot}57AsF_3$ by analysis of tervalent elements iodometrically, total antimony as sulphide, and arsenic as sulphide. When the reactants were in the molar ratio $SbF_5 : SbF_3 = 411 : 1$, the residue was $SbF_3,1{\cdot}09SbF_5,0{\cdot}09AsF_3$.

Conductivity of Fluorosulphonic Acid.—The acid was made by passing sulphur trioxide into excess of hydrogen fluoride. The excess was removed by warming in a stream of nitrogen, and the acid purified by two distillations at normal pressure in an apparatus with the minimum number of ground joints. The fraction of b. p. 163° ± 0·5° was collected, and a middle fraction (range 0·1°) was transferred to a tapless vacuum apparatus where it could be fractionated by trap-to-trap distillation, each trap being sealed in turn. The conductivity cell was connected to the last trap. (Platinum electrodes were joined to the Pyrex glass cell *via* graded seals. This type of seal only withstood one or two experiments before it broke under vacuum. Soft-glass seals held in ground joints were more durable but the most satisfactory arrangement was a platinum–Pyrex seal made vacuum-tight on the inside of the seal with a commercial melamine–formaldehyde resin cured at 200°.) Results were as follows:

Temp.	−78°	−74°	−20°	0°	25·0°	58·4°	25·0°
κ (mhos) × 10^4	0·0727	0·112	0·82	1·38	2·24	5·52	2·52

The attack on glass was indicated by the increased conductivity value at 25° after the measurements above 50°. The activation energy of conduction obtained from the slope of the log κ–$1/T$ plot was 3·83 kcal. The activation energy of viscous flow is between 2·4 and 3·6 kcal. if Trouton's constant is assumed to be 22, and the activation energy of flow between one-third and one-quarter of the latent heat.

Electrolysis of Fluorosulphonic Acid.—The acid was distilled in *via H* (Fig. 1), which was then sealed. The apparatus was evacuated *via A*, the cell being cooled occasionally in liquid air so that the acid remained just molten. The platinum cylinder electrodes were spot-welded to platinum wires which were in turn silver-soldered to tungsten wire–Pyrex glass seals well above the electrolyte level. *E*–*F* and *C*–*B* were gas locks fitted as a precaution against any surge of gas. Once it had been established that gas evolution occurred at only one electrode, the apparatus from *C* to *A*, and tap *D*, were closed off. Electrolyses were initially made at 0° but appreciable amounts of acid vapour were carried over with the gas. This was much reduced by electrolysing at −78° at 20 mA and cooling trap *I* in liquid air for a time at the end of the run. The gas sample was removed in *J*, and its density found by direct weighing, the pressure and volume being known. It was analysed for oxygen in a modified Orsat apparatus, with negative results. The hydrogen content was found by heating it with copper at 300°. A typical analysis follows:

Initial gas pressure at 19·5°, 11·5 cm.; final, 1·7 cm. Weight of water residue 30·0 mg. (Weight of water expected if gas were 100% hydrogen is 29·2 mg. Vapour tension expected for water at 19·5° is 1·7 cm.). The density of the gas was about 3, the high value being due to traces of acid (*ca.* 2%). The volume of gas in the system, approximately estimated because of

temperature differences in the apparatus, was 73·7 ml. at N.T.P. If one Faraday liberates half a molecule of hydrogen, then the 0·2206 g. of copper deposited in a series coulometer would be equivalent to 77·7 ml. Thus, on electrolysis, $H^+ + e^- \longrightarrow \frac{1}{2}H_2$. The percentage of acid electrolysed was 0·5%.

A complete electrolysis, *i.e.*, till gas evolution had ceased, was carried out with a current of 0·2 amp. on 1·5 ml. of acid at −78°, and the gas collected in a calibrated bulb and manometer. The gas evolution had practically ceased in 5 hr.:

Time (hr.)	0	1·0	3·6	5·0	5·85	6·5	9·0	10·15	11·7
Gas pressure (cm.)	0	1·00	2·90	3·45	3·55	3·65	3·55	3·70	3·75

One molecule of acid generated 5560 ml. of hydrogen at N.T.P., which corresponded to 0·25 mole of hydrogen (5600 ml.), *i.e.*, $2HSO_3F = \frac{1}{2}H_2 + HS_2O_6F_2$. The residue had the sweet odour of ozone or fluorine but its aqueous solution did not liberate iodine from iodides or oxidise ferrous or chromic salts. Presumably its oxidising properties were dissipated by liberation of oxygen from water.

Transport of Fluorine in the Acid.—Two simple devices (Fig. 2) were used to separate catholyte from anolyte at the end of electrolysis without the use of taps. In the first the connecting limb was inclined slightly out of the plane through the two compartments. The liquid could be divided by tilting the apparatus to produce a bubble at the constriction. A separation was effected in the second apparatus by pouring off liquid to just below the compartment level. In both apparatus some remixing does occur, especially on prolonged

FIG. 1.

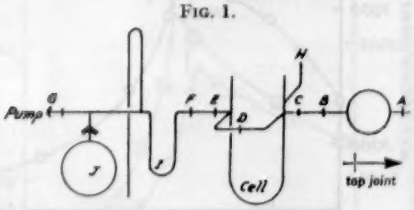
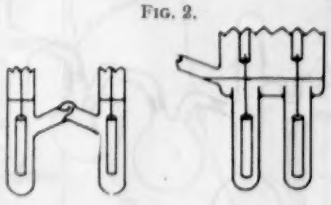


FIG. 2.



electrolysis, so the results are semi-quantitative. For solutions of hydrofluoric acid a cell of the second type in Polythene was used. The fluorine content was found by Willard and Winter's method after hydrolysis of equal volumes from cathode and anode compartments. The results are given in ml. of thorium nitrate solution:

Electrolysis of the acid: anode samples, 261, 262; cathode samples, 248, 249. Electrolysis of hydrogen fluoride (2·60 g.) in fluorosulphonic acid (57·19 g.): anode, 323, 326; cathode, 336, 332. Electrolysis of potassium fluoride (1·78 g.) in the acid (66·13 g.): anode, 243; cathode, 239.

Conductivity of Solutions in Fluorosulphonic Acid.—Potassium fluorosulphonate. The salt was prepared in the dry way from " AnalaR " potassium persulphate and bromine trifluoride, the excess of solvent was removed *in vacuo*, and the powdered residue kept at 150° for 2½ hr. (Found: $KSO_3F/K_2S_2O_8$, 0·510. Calc.: 0·511). The salt, dissolved in water, was free from sulphate, bromide, persulphate, and fluoride. The acid was distilled into *A* at atmospheric pressure (Fig. 3), fractionated *in vacuo* to *B* and *C*, then poured into the cell, which was sealed and weighed. The solvent conductivity was checked, and the salt was then introduced in a stream of dry nitrogen by a weighing tube. The salt dissolved readily in the cold.

100 × Concn. (moles/kg. of solvent)	0	0·460	2·058	3·57	4·415
$10^3\kappa$ (at 25°)	0·495	1·594	5·46	9·00	10·94
(A) Molecular conductivity	—	239	240	241	237
(B) " "	—	346	266	255	248

(A) With solvent correction; (B) without.

The corresponding data for aqueous solution were given in Part I and those for solutions in bromine trifluoride were:

100 × Concn. (moles/kg. of solvent)	2·41	4·93	6·13	8·92
$10^3\kappa$ (at 25°)	11·25	13·10	14·01	15·50
(A) Molecular conductivity	135	116	98	84

(Solvent conductivity = 8·10 × 10^{-3} mho.)

Antimony trifluoride. The trifluoride was purified by Bak and Hillebert's method (*Acta Chem. Scand.*, 1953, **7**, 236) and finally by sublimation. The solvent had to be heated to effect solution.

100 × Concn. (moles/kg. of solvent)	0·681	1·746	3·81	7·30
$10^4\kappa$ (at 25°)	4·99	8·50	13·90	20·62
(A) Molecular conductivity	39·9	36·0	30·7	25·2

Antimony pentafluoride. This was vacuum-distilled into small ampoules which were broken and dropped into the solvent.

100 × Concn. (moles/l.)	2·749	4·34	5·87	8·20
$10^4\kappa$ (at 25°)	30·44	41·75	50·4	61·8
(A) Molecular conductivity	97·6	87·9	79·8	71·0

The molecular conductivity extrapolated to infinite dilution by plotting against the square-root of concentration is 46·5 for the trifluoride and 136 for the pentafluoride.

Sulphur trioxide. Sulphur trioxide, prepared by heating 40% oleum, was purified by distillation from phosphorus pentoxide and finally by fractionation *in vacuo*. Specimens were sealed in ampoules which could be broken magnetically in a tapless apparatus, which included a

FIG. 3.

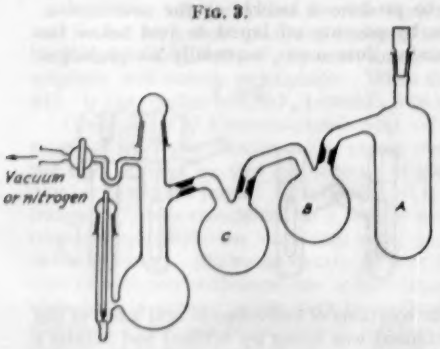
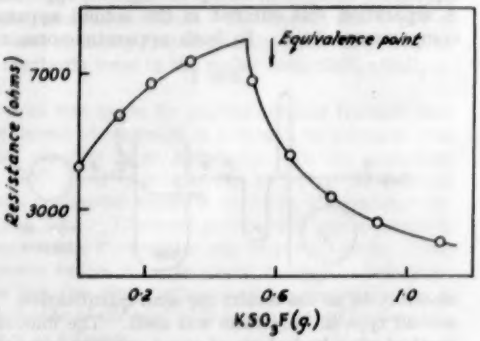


FIG. 4.



purification line for the acid and a conductivity cell. The solvent showed a steady decrease in conductivity on addition of oxide. The solvent required warming to dissolve some of the trioxide which was in the asbestos-like form.

Molar ratio, SO_3/HSO_3F ...	0	0·273	0·550	0·807	0·943	1·243	1·402
$10^4\kappa$ (at 25°)	3·67	1·145	0·816	0·524	0·444	0·332	0·268

Conductometric Titrations.—The vacuum-distillation stage of purification was omitted in the purification of the acid, which consequently had a higher conductivity. Solutions were made by distillation of the solvent into a special type of weighing bottle, followed by addition of solids from weighing tubes, and of liquids either in ampoules or in weight pipettes. The conductivity cell was flushed with dry nitrogen and filled with the solution from one weighing bottle. The titrant was added in portions from another weighing bottle, and the conductivity measured between additions. The titrations are regarded as only approximate, because the solvent was not of the highest purity, the titrant volume was large (a correction has been made in some cases), the solutions and the solvent slowly attack even Pyrex glass, and some fluorides may react irreversibly with the solvent.

Antimony pentafluoride with potassium fluorosulphonate. SbF_5 (0·92 g.) in HSO_3F (89·9 g.). KSO_3F (1·11 g.) in HSO_3F (44·4 g.). The curve is shown in Fig. 4. The initial conductivity was $4·08 \times 10^{-3}$.

Pyridine with antimony pentafluoride. Pyridine (0·89 g.) in HSO_3F (94·6 g.). SbF_5 (4·09 g.) in HSO_3F (84·6 g.). The curve (Fig. 5) was corrected for dilution by multiplying the observed resistances by the factor $V/(V + v)$, where V was the volume of pyridine solution, and v that of titrant.

Nitrobenzene with antimony pentafluoride. $C_6H_5{\cdot}NO_2$ (0·64 g.) in HSO_3F (106·8 g.). SbF_5 (2·44 g.) in HSO_3F (35·2 g.). This curve (Fig. 5) was also corrected.

Auric fluoride with potassium fluorosulphonate. AuF_3 (0·86 g.) in HSO_3F (85·3 g.). KSO_3F (1·31 g.) in HSO_3F (394 g.).

Resistance (ohms) ...	2447	3954	5688	5184	3496	2607	2040	1657	1225
KSO_3F (g.)	0	0·094	0·183	0·361	0·468	0·592	0·742	0·904	1·300

End-point: 0·275 g. of KSO_3F; hence $KSO_3F \approx 2AuF_3$.

Antimony pentafluoride with auric fluoride. SbF_5 (0·587 g.) in HSO_3F (82·3 g.). AuF_3 (1·23 g.) in HSO_3F (84·6 g.).

Resistance (ohms)	6135	4884	3924	3336	3035	2817	2670	2533	2412	2308	2235
AuF_3 (g.)	0	0·113	0·204	0·317	0·410	0·512	0·605	0·720	0·866	1·039	1·229

Arsenic trifluoride with antimony pentafluoride. AsF_3 (0·44 g.) in HSO_3F (92·0 g.). SbF_5 (1·656 g.) in HSO_3F (60·1 g.).

Resistance (ohms)	16,060	18,580	14,098	10,220	6830	6073
SbF_5 (g.)	0	0·221	0·303	0·448	0·785	0·960

End-point at 0·26 g. SbF_5; hence, $SbF_5 \approx 3AsF_3$.

FIG. 5.

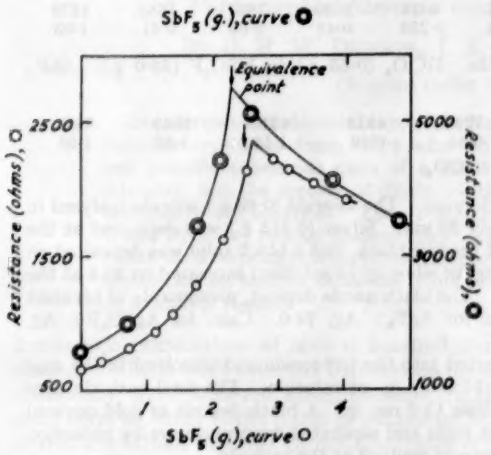
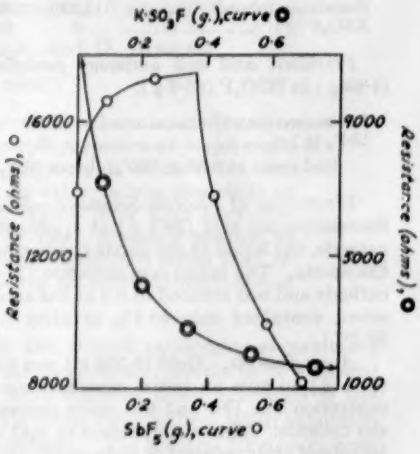


FIG. 6.



Arsenic trifluoride with potassium fluorosulphonate. AsF_3 (0·53 g.) in HSO_3F (97·0 g.). KSO_3F (0·93 g.) in HSO_3F (25·9 g.).

Resistance (ohms)	16,760	5031	2910	1911	1473	1330
KSO_3F (g.)	0	0·156	0·289	0·522	0·794	0·92

Antimony trifluoride with antimony pentafluoride. SbF_3 (0·30 g.) in HSO_3F (109·0 g.). SbF_5 (1·97 g.) in HSO_3F (110·5 g.).

Resistance (ohms) ...	18,500	24,390	25,360	23,170	19,310	16,020	14,030	12,555	11,310
SbF_5 (g.)	0	0·083	0·136	0·21	0·32	0·43	0·51	0·62	0·72

End-point at 0·19 g. SbF_5; hence $SbF_5 \approx 2SbF_3$.

Antimony pentafluoride with tantalum pentafluoride. SbF_5 (0·63 g.) in HSO_3F (89·9 g.). TaF_5 (1·55 g.) in HSO_3F (70·2 g.).

Resistance (ohms) ...	6773	7275	7604	8255	8643	9143	9707	10,430	10,998
TaF_5 (g.)	0	0·116	0·200	0·402	0·538	0·706	0·928	1·244	1·541

Bromine trifluoride with potassium fluorosulphonate and antimony pentafluoride. BrF_3 (0·60 g.) in HSO_3F (88·4 g.). KSO_3F (0·98 g.) in HSO_3F (40·8 g.). BrF_3 (0·46 g.) in HSO_3F (93·4 g.). SbF_5 (1·66 g.) in HSO_3F (60·1 g.).

Both titration curves are shown in Fig. 6.

The end-point is at 0·38 g. SbF_5; hence $SbF_5 \approx 2BrF_3$.

Iodine pentafluoride with potassium fluorosulphonate. IF_5 (0·75 g.) in HSO_3F (98·1 g.). KSO_3F (0·73 g.) in HSO_3F (52·0 g.).

Resistance (ohms)	6175	4228	3334	2944	2166	1892	1627
KSO_3F (g.)	0	0·084	0·160	0·249	0·396	0·54	0·71

Iodine pentafluoride with antimony pentafluoride. IF_5 (0·71 g.) in HSO_3F (88·1 g.). SbF_5 (1·65 g.) in HSO_3F (43·0 g.).

Resistance (ohms)	15,190	24,370	13,680	9700	7241	6396	5480
SbF_5 (g.)	0	0·15	0·41	0·64	1·00	1·22	1·62

End-point at 0·24 g. SbF_5; hence $SbF_5 \approx 3IF_5$.

Platinum tetrafluoride with potassium fluorosulphonate. Because of the low solubility of the tetrafluoride, all that could be shown was a rise in resistance on addition of a small amount of fluorosulphonate solution followed by a decrease on further addition.

Perchloric acid with potassium fluorosulphonate. $HClO_4$ (0·477 g.) in HSO_3F (106·8 g.). KSO_3F (1·04 g.) in HSO_3F (51·1 g.).

Resistance (ohms)	12,390	6894	4024	2522	1937	1685	1470
KSO_3F (g.)	0	0·098	0·235	0·45	0·66	0·81	1·03

Perchloric acid with antimony pentafluoride. $HClO_4$ (0·55 g.) in HSO_3F (56·0 g.). SbF_5 (1·68 g.) in HSO_3F (35·6 g.).

Resistance (ohms)	6670	7290	4922	4310	3940	3827
SbF_5 (g.)	0	0·44	0·89	1·18	1·52	1·66

End-point at 0·58 g. SbF_5; hence $SbF_5 \approx 2HClO_4$.

Electrolyses of Fluoride Solutions.—Silver fluoride. The fluoride (0·69 g.) was electrolysed in fluorosulphonic acid (39·9 g.) at approximately 20 mA. Silver (0·313 g.) was deposited at the cathode, the liquid in the anode compartment became black, and a black solid was deposited on the anode. The initial concentration (14·8 mg. of silver/g. of solution) increased to 20·4 at the cathode and was reduced to 9·2 at the anode. The black anode deposit, presumably of bivalent silver, contained only 40·4% of silver (Calc. for AgF_2: Ag, 74·0. Calc. for $AgSO_3F$: Ag, 52·2%).

Auric fluoride. Gold (0·706 g.) was converted into the trifluoride and dissolved in the acid (41·1 g.) to give an initial concentration of 17·2 mg./g. of solution. The final cathode concentration was 19·1 and the anode concentration 13·8 mg./g. A black deposit of gold covered the cathode. This was dissolved in cold aqua regia and separated from platinum by reduction by quinol after removal of nitric acid. No gas was evolved at the cathode.

Antimony pentafluoride. The pentafluoride (1·26 g.) in fluorosulphonic acid (44·0 g.) was electrolysed at approximately 20 mA until 0·00295 Faraday had passed. Samples were analysed iodometrically for tervalent and total antimony. The latter was precipitated as sulphides and reduced by boiling with concentrated hydrochloric acid. The initial antimony concentration found by analysis was 15·64 mg./g. of solution (Calc.: 15·74 mg./g.). The final concentrations were 17·64 and 13·13 mg./g. at anode and cathode respectively. The antimony balance showed that part had been reduced to Sb^0 and Sb^{III} at the cathode. The deposit on the latter was dissolved in concentrated sulphuric acid for analysis. The results, in mg. of antimony, were:

Anode compartment:	Initial, 313.	Final, 353.
Cathode	,,	,, 317.	,, 277.

The final anode quantity includes 11·5 mg. of Sb^{III}, and the cathode 26 mg. of Sb^{III} and 11 mg. of Sb^0 (electrode deposit).

Antimony trifluoride. A solution (36·4 g.) which contained 10·39 mg. of Sb^{III}/g. was electrolysed at about 12 mA (0·00247 Faraday passed):

Cathode compartment:	Initial, 200.	Final, 209.
Anode	,,	,, 175.	,, 165.

The final anode quantity included 132 mg. of Sb^V, and the cathode 52 mg. of Sb^0 (electrode deposit).

Tantalum pentafluoride. The initial tantalum concentration (15·9 mg./ml.) increased to 17·0 at the anode, and decreased to 14·5 at the cathode. The tantalum precipitated as hydroxide with ammonia was ignited and then extracted repeatedly with hydrofluoric acid to remove silica.

Bromine trifluoride. The trifluoride (1·66 g.) in the acid (54·3 g.) produced no hydrogen on electrolysis. In the catholyte a brown lower layer appeared which moved slowly upwards. Analysis by precipitation of silver bromide showed that the cathode contained more bromine than the anode.

Most of this work was carried out during 1953 when the author was a Turner and Newall Fellow. He is indebted to the Imperial Smelting Corporation for the generous gifts of fluorosulphonic acid used in conductometric titrations.

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Studies in the Synthesis of Cortisone. Part IX. Infra-red Absorption of Polymorphic Steroids and Steroidal Sapogenins.*

By D. H. W. DICKSON, J. E. PAGE, and D. ROGERS.

[Reprint Order No. 5662.]

Six steroids and steroidal sapogenin derivatives have been isolated in more than one crystalline form. The infra-red absorption spectra of Nujol mulls and potassium bromide discs of a steroid's polymorphic forms differ considerably, but the spectra of dilute solutions in either carbon disulphide or bromoform are identical. The differences in crystal form have been confirmed by *X*-ray powder photography. It is desirable, whenever possible, to record for interpretation purposes the spectrum of the solution rather than, or in addition to, that of either the Nujol mull or the potassium bromide disc of an unknown steroid.

INFRA-RED examination of several hundred steroids and steroid sapogenins encountered during synthetic work revealed that certain steroid samples, though known to be identical chemically, gave infra-red absorption spectra that were different when examined in the solid state as either Nujol mulls or potassium bromide discs, but identical when examined as dilute solutions in either carbon disulphide or bromoform. The spectral differences were attributed to polymorphism; this was confirmed by *X*-ray diffraction.

Polymorphic forms of steroids have been recorded, *viz.*, progesterone (Slotta, Ruschig, and Blanke, *Ber.*, 1934, **67**, 1947; Butenandt and Schmidt, *Ber.*, 1934, **67**, 2088), cholest-4-en-3-one (Barton and Jones, *J.*, 1943, 602), 3β-acetoxypregn-5-en-20-one (Gould and Tarpley, *Science*, 1951, **113**, 417), 5-hydroxycholestan-3-one (Fudge, Shoppee, and Summers, *J.*, 1954, 958), 3β-hydroxy*ætio*cholan-17-one (Marker and Rohrmann, *J. Amer. Chem. Soc.*, 1940, **62**, 900), 3β-acetoxy*allo*pregnane-11 : 20-dione (Chamberlin, Ruyle, Erickson, Chemerda, Aliminosa, Erickson, Sita, and Tishler, *ibid.*, 1953, **75**, 3477), cortisone acetate (Merck & Co., Inc., B.P. 694,280), and smilagenin and sarsasapogenin acetates (Marker, Wagner, Ulshafer, Wittbecker, Goldsmith, and Ruof, *J. Amer. Chem. Soc.*, 1943, **65**, 1199; 1947, **69**, 2167), but Merck & Co., Inc., alone presented *X*-ray diffraction evidence for polymorphism (cortisone acetate); no-one has reported infra-red measurements on these compounds.

We believe that infra-red spectroscopy provides a valuable method for identifying polymorphic steroids and is more rapid and more informative than *X*-ray powder photography. Its value for crystalline polymorphs of organic compounds has been demonstrated by Ebert and Gottlieb (*ibid.*, 1952, **74**, 2806), Kendall (*Analyt. Chem.*, 1953, **25**, 382), Ross (*ibid.*, 1953, **25**, 1288), and Plattner, Keller, and Boller (*Helv. Chim. Acta*, 1954,

* Part VIII, *J.*, 1954, 1739.

37, 1379) and of inorganic compounds by Hunt, Wisherd, and Bonham (*Analyt. Chem.*, 1950, **22**, 1478), Keller and Halford (*J. Chem. Phys.*, 1949, **17**, 26), and Wagner and Hornig (*ibid.*, 1950, **18**, 296); Mochel and Hall (*J. Amer. Chem. Soc.*, 1949, **71**, 4082) have observed absorption bands in the spectrum of crystallised neoprene, which are absent from that of the amorphous polymer.

However, care must be exercised in interpreting Nujol mull spectra. Solvent of crystallisation and crystal orientation effects (sometimes complicated by the small inherent polarization of radiation in a prism spectrometer) can produce appreciable changes. Solvent of crystallisation can be detected by analysis, optical rotations, and solution spectra. Crystal orientation effects may be eliminated by fine grinding.

The infra-red measurements discussed below indicate that the two forms of each compound differ in their crystal form. This is confirmed by the *X*-ray data summarised in the Table. *pseudo*Tigogenin illustrates the case of solvent of crystallisation: the other five examples are of true polymorphism.

The possibility of polymorphism provides an additional reason for recording for interpretation purposes, whenever possible, the solution spectrum rather than, or in addition to, the Nujol mull or potassium bromide disc spectrum of a compound. Jones and Dobriner (*Vitamins and Hormones*, 1949, **7**, 293; see also Cole, *Chem. and Ind.*, 1954, 661) stressed the desirability of examining steroids as dilute solutions and, from a study of such spectra, have drawn up frequency correlation tables for the principal oxygen-containing groups, unsaturated linkages, and stereochemical configurations in steroids (see Jones and Herling, *J. Org. Chem.*, 1954, **19**, 1252). Because of intermolecular hydrogen-bonding effects, however, these correlations cannot be trusted if the spectral measurements are conducted on samples in the solid state. Thus the absence of a band at 1746 cm.$^{-1}$ and the presence of one at 1730 cm.$^{-1}$ in the Nujol mull spectrum of the B-form of *allo*-4 : 5-dihydrocortisone acetate (see Figure) suggests that the compound does not contain a 21-acetate group but possibly contains a 3-acetate group. Again the 1000—800-cm.$^{-1}$ region of the Nujol mull spectrum of the B-form of *pseudo*tigogenin (C.S. no. 151 *) suggests a new type of sapogenin rather than a *pseudo*sapogenin. Solution spectra show that these interpretations are incorrect.

Experimental

The spectroscopic measurements were made with a Perkin–Elmer Corporation model 21, double-beam, infra-red spectrophotometer fitted with a sodium chloride prism and were conducted over the spectral range 4000—650 cm.$^{-1}$. The accuracy of frequency measurements for sharp maxima was about ± 3 at 1700 and ± 2 cm.$^{-1}$ at 800 cm.$^{-1}$.

The Nujol mulls were prepared by grinding about 5 mg. of the compound to a fine powder and mulling it with one drop of Nujol to give a thick smooth paste, and the potassium bromide discs by grinding about 2 mg. of the compound with 300 mg. of dry powdered "AnalaR" potassium bromide and then pressing the mixture under a vacuum to give a transparent disc (cf. Stimson and O'Donnell, *J. Amer. Chem. Soc.*, 1952, **74**, 1805). Compounds that were sufficiently soluble were examined as 1·0% (w/v) carbon disulphide and carbon tetrachloride solutions in 1·0-mm. cells; the less soluble compounds were examined as 1·0% (w/v) redistilled bromoform solutions in 1·0-mm. cells. Compensation for solvent absorption was achieved by passing the reference beam of the instrument through pure solvent in a matched cell.

The *X*-ray diffraction patterns were photographed with a Unicam 19-cm. powder camera by means of copper $K\alpha$ radiation. The interplanar spacings in Å for the three strongest diffraction lines are listed in the Table in order of decreasing intensity.†

All the compounds examined had been prepared in these laboratories (see previous and subsequent papers in the present series). Optical rotations were measured for chloroform solutions in a 1-dm. tube at room temperature (20—25°) unless otherwise stated.

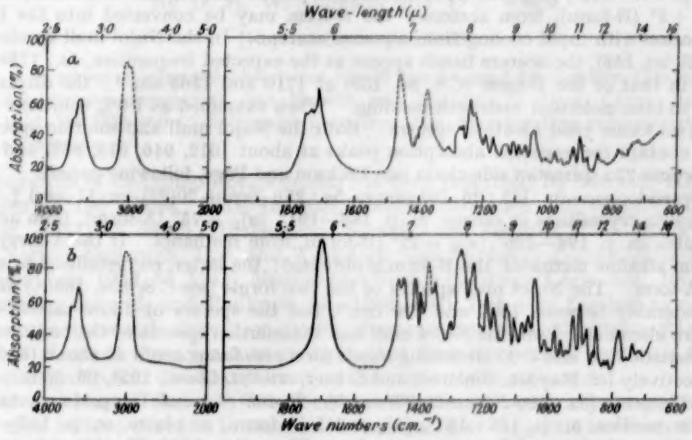
* Spectra thus marked are deposited with the Chemical Society. Photocopies may be obtained, price 3*s.* 0*d.* per copy per spectrum, on application, quoting the C.S. no., to the General Secretary, The Chemical Society, Burlington House, Piccadilly, London, W.1.

† The *X*-ray powder values for each of these substances are being included in full in a forthcoming supplement to the A.S.T.M. Index. Until this is published the values may be had from the authors upon request.

Compound	Spacings in Å of three strongest *X*-ray diffraction bands in order of decreasing intensity: A-form	B-form
allo-4 : 5-Dihydrocortisone acetate	5·99, 5·02, 5·61	5·92, 5·56, 4·36
11β-Hydroxytigogenin	6·47, 5·73, 5·31	6·29, 5·62, 5·19
3β-Acetoxy-23*a*-bromo-11β-hydroxy-5α : 22*a*-spirostan-12-one	5·38, 5·71, 6·93	6·62, 5·17, 4·84
11-Oxo*pseudo*tigogenin	5·71, 6·34, 4·57	5·23, 5·75, 4·13
*pseudo*Tigogenin	5·10, 6·39, 5·87	6·03, 5·06, 4·76

3β-*Acetoxy*allo*pregnane*-11 : 20-*dione*.—3β-Acetoxy*allo*pregnane-11 : 20-dione obtained by partial synthesis from hecogenin and recrystallised from aqueous methanol originally gave needles (A-form), m. p. 127—128°, which remelted at 143·5°, $[\alpha]_D$ +88·5°. Material obtained by partial synthesis from ergosterol and recrystallised from aqueous methanol gave plates (B-form), m. p. 142—144°, $[\alpha]_D$ +88·5°. Samples recently prepared from hecogenin were of the B-form. The infra-red spectra of Nujol mulls [see C.S. nos. 152(A) and 153(B)] and of potassium bromide discs of the two forms differ significantly. Thus C=O stretching bands for the acetate and ketone groups of the A-form appear at about 1728 and 1700 cm.$^{-1}$ and those for the B-form

allo-4 : 5-*Dihydrocortisone acetate* :
a, *A-form* (C.S. no. 154); *b*, *B-form* (C.S. no. 155).



at about 1718 and 1706 cm.$^{-1}$, respectively; the C–O stretching bands for the acetate group in the two forms appear at about 1254 and 1244 cm.$^{-1}$ respectively. Further absorption changes are observed between 1200 and 700 cm.$^{-1}$. Nevertheless, both forms gave identical spectra when examined as 1·0% solutions in carbon disulphide and carbon tetrachloride, and had the same optical rotation and gave the same microanalysis.

When the A-form was fused at 135° and recrystallised from aqueous methanol, plates, m. p. 142—144°, were isolated: mulled with Nujol they gave an absorption spectrum identical with that of the B-form; the spectra of carbon disulphide solutions were identical.

The polymorphism of 3β-acetoxy*allo*pregnane-11 : 20-dione has been reported independently by Chamberlin *et al.* (*loc. cit.*), who obtained needles, m. p. 124—127°, and plates, m. p. 135—136°, from aqueous methanol. Their samples had the same optical rotation, $[\alpha]_D$ +86°, and in carbon tetrachloride solution gave identical infra-red spectra. However they did not report infra-red measurements on solid samples. Djerassi, Batres, Romo, and Rosenkranz (*J. Amer. Chem. Soc.*, 1952, **74**, 3634) obtained crystals, m. p. 143—145°, $[\alpha]_D^{20}$ +86·5°, from hexane–acetone.

allo-4 : 5-*Dihydrocortisone Acetate* (21-*Acetoxy*-17α-*hydroxy*allo*pregnane*-3 : 11 : 20-*trione*).—Crystallisation of *allo*-4 : 5-dihydrocortisone acetate from benzene yields long flat needles, m. p. 228—231°, $[\alpha]_D$ +107° (A-form), and from ethyl acetate elongated plates, m. p. 235—236°, $[\alpha]_D$ +109° (B-form); sublimation of either form yields the A-form. Romo, Rosenkranz, Djerassi, and Sondheimer (*ibid.*, 1953, **75**, 1277) obtained crystals, m. p. 232—235°, $[\alpha]_D^{20}$ +82° (in acetone), from acetone. The Nujol mull (see Figure) and potassium bromide

disc spectra of the two forms differ appreciably in the C=O and C–O stretching regions. The A-form shows the characteristic bands for 21-acetate at about 1746 and 1238, for 20-ketone at 1730, and for 3- and 11-ketones at 1700 cm.$^{-1}$; in the B-form, the 21-acetate bands are displaced to about 1730 and 1272 cm.$^{-1}$ and the 3-, 11-, and 20-ketone bands appear at the same frequency, *i.e.*, about 1710 cm.$^{-1}$. Both forms give identical spectra, when examined as 1·0% solutions in bromoform. The displacement of the 21-acetate bands in the Nujol mull spectrum of the B-form is probably due to intermolecular hydrogen-bonding.

11β-*Hydroxytigogenin* (5α : 22*a*-*Spirostan*-3β : 11β-*diol*).*—The A-form of 11β-hydroxytigogenin, obtained as small needles, m. p. 207—208°, $[\alpha]_D$ −55°, from hexane–ether [cf. Djerassi, Batres, Velasco, and Rosenkranz (*ibid.*, 1952, **74**, 1712), who obtained crystals, m. p. 202—204°, $[\alpha]_D^{20}$ −49°, from hexane–ether], gives a Nujol mull spectrum (C.S. no. 156) that differs in the region between 1300 and 700 cm.$^{-1}$ from the corresponding spectrum of the B-form (C.S. no. 157), which is obtained as needles, m. p. 208—212°, $[\alpha]_D$ −56°, from acetone; dilute carbon disulphide solutions of the two forms yield identical spectra. All the spectra contained bands at about 980, 918, 898, and 865 cm.$^{-1}$ characteristic of an *iso*sapogenin (cf. Wall, Eddy, McClennan, and Klumpp, *Analyt. Chem.*, 1952, **24**, 1337; Jones, Katzenellenbogen, and Dobriner, *J. Amer. Chem. Soc.*, 1953, **75**, 158).

3β-*Aceloxy*-23*a*-*bromo*-11β-*hydroxy*-5α : 22*a*-*spirostan*-12-*one*.†—This ketone crystallises as plates, m. p. 209—212°, $[\alpha]_D$ +3° (A-form), from aqueous ethanol and as needles, m. p. 209—212°, $[\alpha]_D$ +3° (B-form), from acetone; the A-form may be converted into the B-form by recrystallisation with rapid cooling from aqueous acetone. In the Nujol mull spectrum of the A-form (C.S. no. 158), the acetate bands appear at the expected frequencies, *i.e.*, 1738 and 1242 cm.$^{-1}$, and in that of the B-form (C.S. no. 159) at 1710 and 1265 cm.$^{-1}$; the displacement is attributed to intermolecular hydrogen-bonding. When examined as 1·0% solutions in bromoform, the two forms yield identical spectra. Both the Nujol mull and solution spectra of the two forms contain the expected absorption peaks at about 1012, 946, 918, 862, and 726 cm.$^{-1}$ for a 23*a*-bromo-22*a*-spirostan side-chain (see Dickson and Page, following paper).

11-*Oxo*pseudo*tigogenin* (3β : 26-*Dihydroxy*-5α : 25D-*furost*-20(22)-*en*-11-*one*).‡—11-Oxo-*pseudo*tigogenin crystallises as prisms, m. p. 188—191°, $[\alpha]_D$ +73° (A-form), from acetone and as flat needles, m. p. 194—196°, $[\alpha]_D$ +75° (B-form), from methanol. If the A-form is recrystallised from alkaline methanol, the B-form is obtained; the latter, recrystallised from acetone, gives the A-form. The Nujol mull spectra of the two forms [see C.S. nos. 160(A) and 161(B)] differ considerably between 1300 and 700 cm.$^{-1}$, but the spectra of dilute carbon disulphide solutions are identical. Both the Nujol mull and the solution spectra of the two forms exhibit the characteristic C=C and C–O stretching bands for a *pseudo*sapogenin at about 1690 and 1025 cm.$^{-1}$, respectively (cf. Hayden, Smeltzer and Scheer, *Analyt. Chem.*, 1954, **26**, 550).

pseudo*Tigogenin* (5α : 25D-*Furost*-20(22)-*ene*-3β : 26-*diol*).—*pseudo*Tigogenin crystallises from methanol as needles, m. p. 185—187°, $[\alpha]_D$ +24° (A-form), or plates, m. p. 185—187°, $[\alpha]_D$ +21° (B-form). Marker and Rohrmann (*J. Amer. Chem. Soc.*, 1940, **62**, 898) obtained crystals, m. p. 193—196°, from aqueous acetone. The Nujol mull spectra of both forms [see C.S. nos. 150(A) and 151(B)] contain C=C stretching bands at about 1690 cm.$^{-1}$ characteristic of a *pseudo*sapogenin, but differ considerably between 1050 and 800 cm.$^{-1}$, where absorption bands characteristic of the spirostan side-chain appear. The spectrum of the A-form contains a strong C–O stretching band at about 1025 cm.$^{-1}$ and no prominent bands between 1000 and 800 cm.$^{-1}$, indicating an open sapogenin side-chain; that of the B-form reveals strong peaks at 983 and 938 cm.$^{-1}$ and was at first believed to represent a new type of sapogenin derivative. However, the two forms when examined as 1·0% solutions in either pyridine or chloroform yield spectra that differ in the intensity of the absorption band at about 1010 cm.$^{-1}$. Bromoform solutions of the two forms yield spectra that also differ only in the intensity of the peak at about 1015 cm.$^{-1}$,

* Scheer, Kostic, and Mosettig (*J. Amer. Chem. Soc.*, 1953, **75**, 4871) have shown that sarsasapogenin and smilagenin differ in their configurations at $C_{(22)}$ and possibly not, as earlier thought, at $C_{(22)}$. Although this finding casts some doubt on the nature of the isomerism of other sapogenins the conventional name " 22*a*-spirostan " has been used for the *iso*sapogenins.

† Since there is no convention on the representation of steroisomerism at $C_{(23)}$ in the 23-bromo-22*a*-spirostan, the nomenclature proposed by Mueller and Norton (*J. Amer. Chem. Soc.*, 1954, **76**, 749) has been adopted; thus 23-bromo- and 23-*iso*bromo-*iso*sapogenin are designated 23*a*-bromo- and 23*b*-bromo-22*a*-spirostan, respectively.

‡ In order to represent stereoisomerism at $C_{(25)}$ n the furostendiols, the configuration, 25*D*, determined for hecogenin, diosgenin, and smilagenin (James, *Chem. and Ind.*, 1953, 1388), has been assumed for 22*a*-spirostan derivatives; consequently, 22*b*-spirostan derivatives would be 25*L* (cf. Scheer, Kostic, and Mosettig, *loc. cit.*).

but are characteristic of *ana*tigogenin (cf. Dickson, Elks, Evans, Long, Oughton, and Page, *Chem. and Ind.*, 1954, 692) rather than *pseudo*tigogenin; thus the band at about 1690 cm.$^{-1}$ has been replaced by new bands at about 956, 920, and 895 cm.$^{-1}$, the change being induced by a trace of acid in the bromoform. The intensity of the 1010—1015 cm.$^{-1}$ band is greater in the spectrum of the B-form and is attributed to methanol of crystallisation. This deduction is supported by small differences in optical rotation and microanalysis. The methanol of crystallisation must therefore cause the new crystal structure and, through intermolecular hydrogen-bonding, induce the modified spirostan spectrum.

We are indebted to Miss I. E. Lewis for the *X*-ray measurements.

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Studies in the Synthesis of Cortisone. Part X. Infra-red Absorption of* 23a- *and* 23b-*Bromo-*iso*sapogenins.*

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A series of infra-red absorption bands can be used to identify 23*a*- and 23*b*-bromo-*iso*sapogenins (see Mueller and Norton, *J. Amer. Chem. Soc.*, 1954, **76**, 749) and to distinguish them from the corresponding unbrominated sapogenins.

THE preparation of 23-bromo-*iso*sapogenins has been described by Djerassi, Martinez, and Rosenkranz (*J. Org. Chem.*, 1951, **16**, 303), Mueller, Stobaugh, and Winniford (*J. Amer. Chem. Soc.*, 1951, **73**, 2400), Hirschmann, Snoddy, and Wendler (*ibid.*, 1953, **75**, 3252), Mueller, Norton, Stobaugh, Tsai, and Winniford (*ibid.*, p. 4892), Schmidlin and Wettstein (*Helv. Chim. Acta*, 1953, **36**, 1241), Mueller and Norton (*J. Amer. Chem. Soc.*, 1954, **76**, 749), and Cornforth, Osbond, and Phillipps, (*J.*, 1954, 907), but only the last-named authors mentioned the infra-red absorption peaks characteristic of a 23*a*-bromo-22*a*-spirostan. Cornforth *et al.* quote these peaks as evidence that their compounds contain a 23*a*-bromo-22*a*-spirostan group, but do not comment on the origin of the assignment.

Mueller and Norton (*loc. cit.*) described a new series of isomeric bromo-*iso*sapogenins, in which they believe that the bromine atom is located at $C_{(23)}$, but in which the carbon–bromine linkage has a different configuration from that in the original 23-bromo-*iso*-sapogenins; the latter were provisionally designated 23*a*-bromo-22*a*-spirostans in order to distinguish them from the new compounds, which were termed 23*b*-bromo-22*a*-spirostans. Mueller and Norton distinguished chemically between the two groups of isomers, but did not offer any infra-red evidence. We have found that the infra-red spectra of the two groups differ considerably in the 1050—850-cm.$^{-1}$ region, and we have identified absorption bands characteristic of the 23*a*- and 23*b*-bromo-isomers and available for distinguishing them from the corresponding unbrominated *iso*sapogenins.

EXPERIMENTAL

The spectroscopic measurements were conducted as described by Dickson, Page, and Rogers.* Compounds sufficiently soluble in carbon disulphide and carbon tetrachloride were examined as 1·0% (w/v) solutions in 1·0-mm. thick sodium chloride cells. Compounds that were insoluble in carbon disulphide were examined, if soluble, as 1·0% (w/v) solutions in solvents such as bromoform, chloroform, methylene chloride, and pyridine, or as Nujol mulls. Absorption intensities were measured as apparent molecular extinction coefficients calculated from the relationship: $\varepsilon = 1/cl \log_{10} (T_0/T)$, where T_0 and T are respectively the % radiation transmitted by the solvent and by the solution at the frequency of the absorption peak, c is the solute concentration in moles per l. and l is the cell thickness in cm.

* Part IX, preceding paper.

The results are tabulated.

The 23*a*- and 23*b*-bromo-*iso*sapogenins, which had been prepared in these laboratories (see previous and subsequent papers in the present series), had the properties given below, references being: (*a*) Cornforth *et al.*, (*b*) Schmidlin and Wettstein, (*c*) Mueller and Norton, (*d*) Mueller, Norton, Stobaugh, Tsai, and Winniford, *locc. cit.*:

(1) 23*a*-Bromo-3β-hydroxy-5α : 22*a*-spirostan-12-one (I), m. p. 205° (decomp.) (*a*).

(2) 3-Acetate of (I), m. p. 225—227° (*a*) [cf. m. p. 227—228° (decomp.) (*b*)].

(3) 23*a*-Bromo-11β : 12β-epoxy-5α : 22*a*-spirostan-3β-ol, m. p. 207—209° (*a*).

(4) 3-Acetate of (3), m. p. 233—235° (*a*) [cf. m. p. 232—234° (decomp.) (*b*)].

(5) 23*a*-Bromo-12-oxo-5α : 22*a*-spirost-9(11)-en-3β-yl acetate, m. p. 228° (decomp.) [cf. m. p. 220—220·5° (decomp.) (*c*)].

(6) 11α : 23*a*-Dibromo-3β-hydroxy-5α : 22*a*-spirostan-12-one, m. p. 180° (decomp.).

(7) 3-Acetate of (6), m. p. 189—191° (decomp.) (*a*) [cf. m. p. 198—199° (decomp.) (*d*), 180—183° (decomp.) (*c*)].

(8) 11α : 23*a*-Dibromo-12β-hydroxy-5α : 22*a*-spirostan-3β-yl acetate, m. p. 197—202° (decomp.) (*a*) [cf. m. p. 205—206·5° (decomp.) (*b*)].

(9) 11α : 23*a*-Dibromo-12α-hydroxy-5α : 22*a*-spirostan-3β-yl acetate, m. p. 198° (decomp.) (*a*).

(10) 23*a*-Bromo-3β : 12β-dihydroxy-5α : 22*a*-spirostan-11-one, m. p. 208° (decomp.) [cf. m. p. 233—234° (decomp.) (*d*)].

(11) 3 : 12-Diacetate of (10), m. p. 195—196°.

(12) 3β : 12α-Diacetoxy-23*a*-bromo-5α : 22*a*-spirostan-11-one, m. p. 168—171°.

(13) 12α : 23*a*-Dibromo-11-oxo-5α : 22*a*-spirostan-3β-yl acetate, m. p. 229—232° (decomp.) (*a*).

(14) 12α : 23*a*-Dibromo-11β-hydroxy-5α : 22*a*-spirostan-3β-yl acetate, m. p. 233—236° (decomp.) (*a*) [cf. m. p. 237—239° (decomp.) (*b*)].

(15) 23*a*-Bromo-12α-chloro-11β-hydroxy-5α : 22*a*-spirostan-3β-yl acetate, m. p. 233—235° (decomp.) [cf. m. p. 236·5—242° (decomp.) (*b*)].

(16) 23*a*-Bromo-12α-chloro-11-oxo-5α : 22*a*-spirostan-3β-yl acetate, m. p. 230° (decomp.) [cf. m. p. 233—236° (decomp.) (*b*)].

(17) 23*b*-Bromo-12-oxo-5α : 22*a*-spirost-9(11)-en-3β-yl acetate, m. p. 220° (decomp.) [cf. m. p. 220—221° (*c*)].

(18) 11α : 23*b*-Dibromo-12-oxo-5α : 22*a*-spirostan-3β-yl acetate, m. p. 168—169° (decomp.).

Discussion

The strong peaks in the 1000—720-cm.$^{-1}$ region (see Tables) may be used to identify the two groups of bromo-compounds and to distinguish them from unbrominated 22*a*-

Table 1. *Frequency assignments (cm.$^{-1}$) for* 23a-*bromo*-22a-*spirostans in carbon disulphide solution.**

Compound	Hydroxy	Acetate	Ketone	Chlorine	23*a*-Bromo-22*a*-spirostan
1	3620, 1042	—	1710	—	1010, 947 > 919, 862, 725
2	—	1736, 1240	1712	—	1010, 946 > 920, 860, 724
3	3620, 1035	—	—	—	1010, 945 > 918, 866, 732
4	—	1732, 1240	—	—	1012, 944 > 916, 860, 732
5	—	1736, 1240	1675	—	1010, 945 > 918, 862, 728
6	3620, 1036	—	1730	—	1010, 946 > 918, 862, 726
7	—	1730, 1240	1730	—	1008, 944 > 917, 864, 726
8	3620	1731, 1238	—	—	1010, 944 > 916, 860, 724
9	3620	1736, 1242	—	—	1016, 948 > 917, 860, 724
10 †	3620, 3480	—	1705	—	1014, 944 > 918, 862, 724
11	—	{ 1752, 1220 1730, 1240	1730	—	1010, 946 > 918, 864, 728
12	—	{ 1758, 1218 1735, 1242	1735	—	1010, 945 > 918, 862, 724
13	—	1735, 1242	1710	—	1012, 946 > 916, 865, 728
14	3620	1735, 1238	—	—	1010, 944 > 915, 865, 726
15 †	3560	1717, 1266	—	776	1016, 948 > 918, 864, 728
16	—	1734, 1242	1718	762	1012, 946 > 918, 862, 726

* A dash indicates that an absorption band is absent from the spectrum and, *e.g.*, "947 > 919" that the intensity of the absorption band at 947 cm.$^{-1}$ is greater than that of the band at 919 cm.$^{-1}$.

† As Nujol mull.

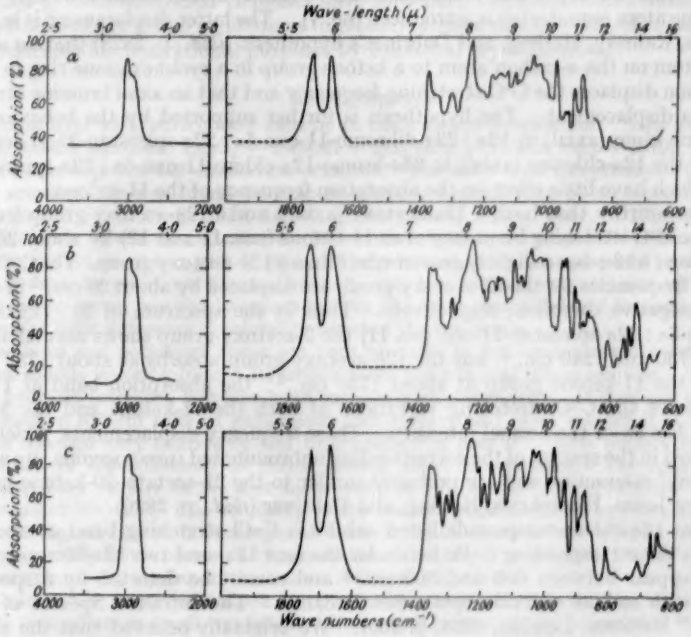
spirostans. 23*a*-Bromo-22*a*-spirostans absorb at about 1012, 946, 918, 862, and 726 cm.$^{-1}$ and 23*b*-bromo-22*a*-spirostans at about 1015, 972, 943, 905, and 880 cm.$^{-1}$; in the former compounds the absorption peak at 946 cm.$^{-1}$ (ε 320—250) is considerably stronger

TABLE 2. *Frequency assignments (cm.$^{-1}$) for 23b-bromo-22a-spirostans in carbon disulphide solution.*

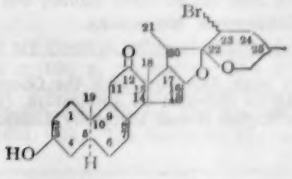
Compound	Acetate	Ketone	23*b*-Bromo-22*a*-spirostan
17	1736, 1240	1676	1013, 972, 944, 910, 878
18	1732, 1240	1732	1015, 972, 943, 904, 882

than that at 918 cm.$^{-1}$ (ε 140—100) and in the 23*b*-isomers the peak at 972 cm.$^{-1}$ (ε about 450) is considerably stronger than that at 943 cm.$^{-1}$ (ε about 150). These absorption peaks have the same relative intensities in Nujol mull and carbon disulphide, carbon tetra-

Infra-red spectra of (*a*) 12-*oxo*-5α : 22a-9(11)-*en*-3β-*yl acetate* (*C.S. no.* 164), *and* (*b*) *its* 23a-*bromo*-(*C.S. no.* 165) *and* (*c*) 23b-*bromo-derivative* (*C.S. no.* 166).



chloride, and bromoform solution. The spectra of both bromo-isomers are free from strong peaks at about 980 and 898 cm.$^{-1}$ and are thus readily distinguished from those of unbrominated 22*a*-spirostans, which have peaks at about 980 (ε 440—304), 918 (ε 170—100),



and 898 cm.$^{-1}$ (ε 280—150); (cf. Wall, Eddy, McClennan, and Klumpp, *Analyt. Chem.*, 1952, **24**, 1337; Jones, Katzenellenbogen, and Dobriner, *J. Amer. Chem. Soc.*, 1953, **75**, 158).

The spectra of 12-oxo-5α : 22*a*-spirost-9(11)-en-3β-yl acetate and its 23*a*- and 23*b*-bromo-derivatives may be compared in the Figure. Similar relations are shown by hecogenin acetate (C.S. no. 162) and its 23*a*-bromo-derivative (C.S. no. 163).*

The 1350—1500-cm.$^{-1}$ region of the spectrum of a steroid in carbon tetrachloride solution provides information on the individual methyl and methylene groups (Jones and Cole, *ibid.*, 1952, **74** 5648; Jones, Cole, and Nolin, *ibid.*, p. 5662) and it was thought that the spectra now available might indicate the location and conformation of the bromine atom. This, however, is not possible.

The spectra summarised in the Tables show that substituents in rings A, B, and C of a 23-bromo-22*a*-spirostan absorb at their normal frequencies. The displaced acetoxy C=O (from 1732 to 1717 cm.$^{-1}$) and C–O stretching frequencies (from 1240 to 1266 cm.$^{-1}$) in the Nujol mull spectrum of 23*a*-bromo-12α-chloro-11β-hydroxy-5α : 22*a*-spirostan-3β-yl acetate are attributed to intermolecular hydrogen bonding.

A 12-ketone (*e.g.*, no. 2), that normally absorbs at about 1712 cm.$^{-1}$, absorbs at about 1675 cm.$^{-1}$ when a 9(11)-double bond is introduced (no. 5) and at about 1730 cm.$^{-1}$ when an 11*a*-bromine atom (equatorial) is introduced (no. 7). The latter displacement is in harmony with Jones, Ramsay, Herling, and Dobriner's hypothesis (*ibid.*, p. 2828) that an equatorial bromine atom on the α-carbon atom to a ketone group in a *cyclo*hexanone ring in the chair configuration displaces the C=O stretching frequency and that an axial bromine atom causes little or no displacement. The hypothesis is further supported by the behaviour of the 12*a*-bromine atom (axial) in 12α : 23*a*-dibromo-11-oxo-5α : 22*a*-spirostan-3β-yl acetate (no. 13) and of the 12α-chlorine (axial) in 23*a*-bromo-12α-chloro-11-oxo-5α : 22*a*-spirostan-3β-yl acetate, which have little effect on the absorption frequency of the 11-ketone.

It is noteworthy that both a 12α-acetoxy (axial), and a 12β-acetoxy-group (equatorial) displace the C=O stretching frequency of an 11-ketone (nos. 11 and 12) by about 25 cm.$^{-1}$ to higher values; a 12α- has a slightly greater effect than a 12β-acetoxy group. The C=O and C–O stretching frequencies for the 12-acetoxy-group are displaced by about 20 cm.$^{-1}$ in a positive and in a negative direction, respectively. Thus in the spectrum of 3β : 12β-diacetoxy-23*a*-bromo-5α : 22*a*-spirostan-11-one (no. 11) the 3-acetoxy-group shows normal absorption at about 1730 and 1240 cm.$^{-1}$, but the 12β-acetoxy-group absorbs at about 1752 and 1220 cm.$^{-1}$ and the 11-ketone group at about 1730 cm.$^{-1}$; the absorption band at 1730 cm.$^{-1}$ accommodates the C=O stretching vibrations of both the 11-ketone and the 3-acetoxy-group and has twice the normal intensity. These frequency displacements, which we have also observed in the spectra of the corresponding unbrominated *iso*sapogenins, are attributed to dicarbonyl interaction and are probably similar to the 21-acetate–20-ketone interaction reported by Jones, Humphries, Herling, and Dobriner (*ibid.*, p. 2820).

The two 12α-chloro-compounds listed exhibit a C–Cl stretching band at about 760—775 cm.$^{-1}$; the corresponding C–Br bands for the four 11α- and two 12α-bromo-compounds probably appear between 600 and 500 cm.$^{-1}$ and cannot be detected by a spectrometer equipped with sodium chloride optics (see Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 269). We originally believed that the absorption band at about 726 cm.$^{-1}$ in the spectrum of a 23*a*-bromo-22*a*-spirostan was associated with a C–Br stretching vibration, but it was later found that the band does not appear in the spectrum of a 23*b*-bromo-22*a*-spirostan; the absence of the band in the latter compounds may, however, be due to the different configuration of the C–Br linkage.

GLAXO LABORATORIES, LTD., GREENFORD, MIDDLESEX. [*Received, August 19th*, 1954.]

* Spectra thus designated have been deposited with the Chemical Society. Photocopies, price 3*s.* 0*d.* per copy per spectrum, may be obtained on application, citing the C.S. no., to the General Secretary, the Chemical Society, Burlington House, Piccadilly, London, W.1.

The Separation of the Lanthanons with the Aid of Ethylenediaminetetra-acetic Acid ("Enta Acid"). Part V. The Solubilities of Some Alkali Lanthanon Enta Salts.*

By J. K. Marsh.

[Reprint Order No. 5732.]

Sodium lanthanon enta salts show a range of solubilities increasing by up to 18-fold from gadolinium to erbium. The behaviour of the potassium salts is similar but the range is smaller. Both series are readily crystallised. In the cerium group the solubility differences are small.

The probability that the sodium lanthanon ethylenediaminetetra-acetates would prove useful for fractional crystallisation purposes was indicated in Part III (*J.*, 1951, 3057). Solubilities of even-numbered elements have now been determined and indicate that, of all known salts of the group gadolinium to erbium (atomic nos. 64—68), these are much the most favourable for separational purposes by fractional crystallisation.

Experimental

Oxides of over 99% purity were used in all cases except dysprosium. Salts were prepared according to the equation, $Ln_2O_3 + 2NaOH + 2H_4$ enta $= 2NaLn$ enta $+ 5H_2O$, by warming the ingredients together till dissolution occurred. The salts were recrystallised from slightly alkaline solution. It was found possible to prepare sodium salts of an isomorphous series (Moeller, *Record Chem. Prog.*, 1953, **14**, 69, quoting Moss, Thesis, Univ. of Illinois, 1952) over the range cerium to erbium (atomic nos. 58—68) but lanthanum gave a different salt, and the ytterbium product dried to a gum or glass. The potassium salts were prepared for the members from lanthanum to ytterbium (atomic nos. 57—70), but yttrium, erbium, and ytterbium salts occurred in two forms, one nearly square tablets, the other pyramidal and inclined to effloresce. There seemed little difference in solubility between the two forms.

The sodium and potassium series are both unstable in hot concentrated solution, passing into a less soluble lower hydrate. Reversion takes place in cold dilute solution. The stability of lower hydrates increases, however, with increasing atomic weight. It does not cause trouble in fractionating sodium salts of gadolinium and dysprosium; with erbium it is necessary to warm the solution very cautiously and to crystallise it near 0°. Rest periods for reversion, or restriction of crystallisation to thrice weekly, may be necessary. The freshly prepared erbium salts may require to be kept for a week or two in cold dilute solution before being concentrated at 30—40°. The solubility of the sodium ytterbium salt appears to be infinite, but it readily gives rise to the amorphous lower hydrate which is less soluble. All the lower hydrates are bulky solids useless for fractionation. Attempts to prepare lithium salts resulted in products physically similar to the sodium salt lower hydrates.

The solubilities were determined by preparing warm solutions of the salts with some remaining solid phase in small test-tubes. These were stoppered and placed in a thermostat at 25° or 35°, or a refrigerator at 2°. Equilibrium was attained after 40 hr., as shown by duplicate results. 1-ml. portions were removed, placed on watch-glasses, and dried *in vacuo*. Constant weights were obtained in 4—5 hr., though further very gradual loss of combined water might occur with prolonged desiccation. Accuracy within 2% was considered sufficient for the purpose of this study, and a few results seen to fit well into the expected trend were not duplicated.

In the Table the solubilities are given in terms of g. of hydrated salt per l. and for gadolinium and erbium also in terms of g./100 g. of water. The latter have been calculated in an approximate manner following determinations of the salt densities by flotation in alcohol–bromoform mixtures. The densities found for the hydrated enta salts were: K Er, 2·00; K Dy, 1·95; Na Dy, 1·94; Na Gd, 1·94. The factor for the increase in solubility in passing from Gd to Er is also indicated.

Discussion.—The phenomenal range of solubility between sodium gadolinium enta and sodium ytterbium enta is at once apparent from the Table. This, coupled with the ease of

* Part IV, *J.*, 1952, 4864.

preparation and crystallisation of salts at least as far down the series as erbium, raises fractional crystallisation to a new level of efficiency for the middle range of the lanthanons.

Solubilities of alkali lanthanon enta salts (g./l.).

Alkali	Temp.	La	Ce	Pr	Nd	Sm	Gd	Dy	Y	Er	Yb
Na	2°	120	28	18	11·8	10·6	11·7	46	97	196	∞
„	25	139	70	42	31	29	36	133	260	450	∞
„	35	—	—	—	49	43	56	199	342	589	∞
K	2	58	—	19·6	17·6	17·9	26	86	220	207	167
„	25	182	—	66	53	54	81	273	443	435	—
„	35	292	—	—	90	96	126	403	523	550	—
* Na	2	—	—	—	—	—	1·18	(— × 18·5 ⟶)		21·8	—
* „	35	—	—	—	—	—	5·7	(— × 14·8 ⟶)		84·3	—
* K	2	—	—	—	—	—	2·64	(— × 8·8 ⟶)		23·2	—
* „	35	—	—	—	—	—	13·5	(— × 5·6 ⟶)		76·5	—

Also NH_4 Gd enta hydrate at 2° 86 g./l.; at 25° 240 g./l.
* In g./100 g. of water.

The much used bromate fractionation depends on an increase of solubilities from gadolinium to ytterbium from 110·5 to 351 g./100 g. of water at 25°, a factor of only 3·17. On a molecular solubility basis the increase from gadolinium to yttrium by bromates is a factor of 1·57 at 25°, by sodium enta salt it is 8·0. The dimethyl phosphates have hitherto been the salts with the greatest known range of solubility, amounting to 5·36-fold at 0° or 7·75-fold at 50° for gadolinium over erbium (Marsh, *J.*, 1939, 554), but their use is not practicable on a large scale.

The Dyson Perrins Laboratory, Oxford. [*Received, September 16th*, 1954.]

The Conductivity of Anhydrous Aluminium Bromide in Ethyl Bromide Solution.

By Fred Fairbrother and Norman Scott.

[Reprint Order No. 5763.]

The conductivity of aluminium bromide in dry ethyl bromide solution, at 25°, has been measured in a totally enclosed system. The molar conductivity is of the order of 10^{-2} to 10^{-1} mho, most of which is due to the ionic dissociation of the aluminium bromide, probably into solvated $AlBr_2^+$ and $AlBr_4^-$. The conductivity of the solutions increases steadily with time, owing to the decomposition of the ethyl bromide–aluminium bromide complex into olefin and hydrogen bromide.

One piece of evidence which is frequently cited in support of the ionisation of an organic halide by an aluminium halide is the electrical conductivity shown by solutions of aluminium bromide in ethyl bromide, especially through the measurements of Wertyporoch (*Ber.*, 1931, **64**, 1369). Whilst denying neither the fact of the conductivity nor the concept of the ionisation, we felt that there was some doubt as to whether the conductivity was indeed experimental evidence of the ionisation of the ethyl bromide.

Since the experimental details and final results given by Wertyporoch (*loc. cit.*) do not indicate that any rigorous precautions had been taken to exclude traces of moisture, and since later work has so clearly emphasised the importance of this in all work with aluminium halides, the conductivity of anhydrous aluminium bromide in dry ethyl bromide has now been measured in a closed system, under strictly anhydrous conditions and over a greater range of concentrations. The results show a number of features which differ from those recorded by Wertyporoch.

Wertyporoch records that in dilute solution (up to 1·5% of $AlBr_3$) the conductivity rose

with time, attaining a limiting value, in 30—45 minutes, of up to five times the initial value. In solutions containing about 5% of $AlBr_3$ the maximum was reached, at about $1\frac{1}{2}$ times the initial value, after 10 minutes, whilst in 10% solution the final value was reached immediately. The final values of the molar conductivities were almost independent of the concentration.

In the present work, which covered a range of concentrations from 0·34 to 15·9% by weight of aluminium bromide, the conductivity in the freshly prepared solutions was less (by a factor of $1\frac{1}{2}$—2 in equivalent concentrations) than that recorded above, whilst the increase was much slower and smaller in amount, provided that the solution was rigorously dry. In one solution (1·1% of $AlBr_3$) the rise of conductivity was followed for six days without reaching a limiting value. Examination of solutions which had been allowed to stand showed the presence both of free hydrogen bromide, which could be volatilised off with the ethyl bromide, and of unsaturated compounds in the liquid. It seems most probable that this increase in conductivity is chiefly due to the hydrogen bromide which originates from the decomposition of a C_2H_5Br–$AlBr_3$ complex, evidence for the formation of which has been given by Brown and Wallace (*J. Amer. Chem. Soc.*, 1953, **75**, 6279). The instability of solutions of aluminium bromide in ethyl bromide has been noted by other workers; *e.g.*, Brown and Wallace (*loc. cit.*) were unable to determine the molecular weight of the solute by vapour-pressure lowering, on account of the slow evolution of hydrogen bromide. They state, however, that their solutions were yellow, as were also those described by Wertyporoch. In the present work all solutions for which results are recorded were colourless: in fact, the absence of colour may be used as a criterion of purity. In a few other experiments, when probably by some accident the drying had been insufficient, the colour was yellow. In these solutions the initial conductivity was slightly greater and increased much faster than in the colourless solutions: these results are not recorded. Since, under these conditions, the hydrolysis of aluminium bromide is very slow (Fairbrother and Frith, *J.*, 1953, 2975) and in any case the amount of water initially present would be too small to account for the hydrogen bromide, it seems that the decomposition of the carbonium ion complex, $C_2H_5^+AlBr_4^-$, is catalysed by a trace of moisture.

Experimental

Ethyl bromide was purified by a method similar to that used by Smith (*J.*, 1931, 2573). A commercial product was mechanically shaken with cold concentrated sulphuric acid for several days, washed, and dried, first with calcium chloride and then with lithium hydride, and fractionated through a Fenske column; it then had b. p. 37·7°/746 mm. Aluminium bromide was prepared by direct synthesis from the elements, refluxed over aluminium turnings until all trace of colour had disappeared, distilled, and purified by seven sublimations *in vacuo*, at the end of which it was transferred, whilst still *in vacuo*, into fragile hook-ended ampoules.

The conductivity cell is shown in Fig. 1. The electrode assembly *E* consisted of two bright platinum plates, 2 × 2 cm., and 0·5 mm. thick, spaced about 2 mm. apart by fused glass beads. Several electrode assemblies were used during the work, the cell constants (by KCl calibration) varying between 0·0330 and 0·0449. The resistance of the solution did not vary with the amount of solution in the cell, provided this exceeded about 50 c.c.

The cell was constructed of Pyrex glass, the stout platinum electrode connections being sealed through short lengths of soda-glass which in turn were sealed to the Pyrex glass by graded seals. This quite overcame the difficulty of vacuum-tight seals associated with platinum sealed through Pyrex glass.

The cell was thoroughly evacuated and out-gassed through *C* which was then sealed, and cooled to −78°, pure aluminium bromide then being sublimed into it, without residue, from the weighed ampoule *A*. The tube *B* containing the broken fragments of the ampoule was removed at *D*. Dry ethyl bromide vapour was then admitted through *F* until about 50 c.c. of ethyl bromide (which is still liquid at −78°) had collected about the electrode assembly. After being sealed off at *F*, the cell was removed from the carbon dioxide bath and lowered into position in a large, well-stirred, water-thermostat at 25°, and the magnetic stirrer *S* rotated by a magnet outside and below the thermostat. The sequence of operations, from removal from the cooling bath to the completion of the first measurement, was timed and averaged about 4 min.

Resistance measurements were made, at 1000 c.p.s., with the usual a.c. Wheatstone's bridge and a visual null-point indicator. The latter was a highly sensitive modification of that described by Hazseldine and Woolf (*Chem. and Ind.*, 1950, 544) with a discrimination of the order of 1 in 10,000. Since both resistance and capacity out-of-balance were indicated separately by this arrangement, it could be observed that no polarisation difficulties were encountered by the use of bright platinum electrodes.

Readings of the resistance were made every 1—2 min. over a period of 30 min. After the first 8—10 min., which were required for attainment of temperature and composition equilibrium,

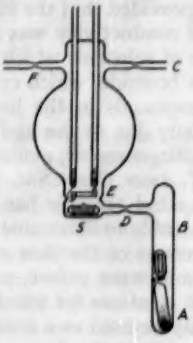


FIG. 1. *The conductivity cell.*

FIG. 2. *Molar conductivities of aluminium bromide–ethyl bromide solutions.*

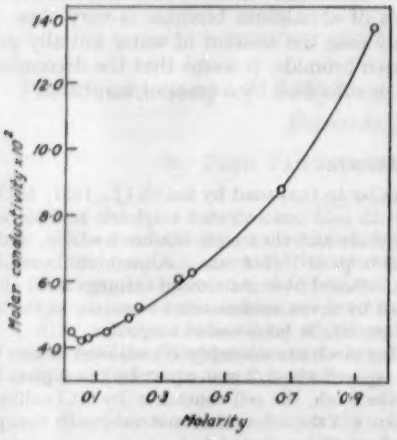
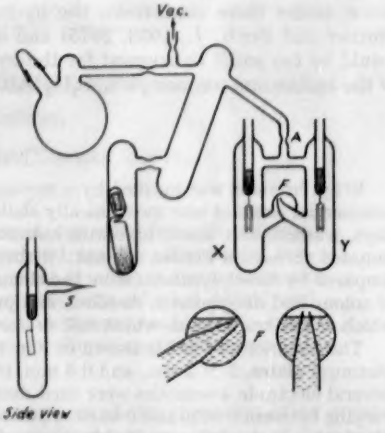


FIG. 3. *Apparatus for transport experiments.*



the decrease of resistance with time became linear, which greatly facilitated extrapolation to zero time of preparation. This was taken as half way between the time of removal of the cell from the cooling mixture and the time of the first measurement; experiment showed that there was no variation of resistance over several minutes at −78°. The decrease in resistance during the first 30 min. varied between 0·069 and 0·255 of the average value for the period. The values recorded are those at zero time of mixing, obtained by extrapolation.

The weight concentrations of the solutions were obtained from the weight of aluminium bromide in the sealed ampoule and the weight of the electrode vessel empty and containing the solution. The volume concentrations (for the calculation of molar conductivities) were obtained from these with the aid of a separate series of pycnometric determinations of the densities of aluminium bromide–ethyl bromide solutions. The latter incidentally showed that aluminium bromide (d_4^{25} 3·01) dissolves in ethyl bromide with less than 1% contraction in total volume over this range.

The weight percentages (g. of $AlBr_3$/100 g. of solution) and specific conductivities are given in the following table. The molar conductivities are shown in Fig. 2.

$AlBr_3$, g./100 g. of soln.	0·3414	0·9361	1·285	2·339	3·570	4·094	6·246	6·899	11·44	15·90
Spec. conductivity (mho) $\times 10^5$	0·084	0·216	0·302	0·578	0·972	1·19	2·14	2·45	5·85	13·0

Jacober and Kraus (*J. Amer. Chem. Soc.*, 1949, **71**, 2405) observed that the molar conductivity of aluminium bromide in methyl bromide at 0° and at −78° is of the order of $2—3 \times 10^{-3}$ mho, indicating an ionic dissociation of order 10^{-4}. In the present work the conductivity in ethyl bromide solutions of similar concentrations was found to be only slightly higher : it is therefore apparent that even the total ionic strength is very low. The form of the conductivity curve, with a clear minimum at about 0·04M (Fig. 2), is of the general type for a weak electrolyte in a solvent of low dielectric constant, discussed by Fuoss and Kraus (*ibid.*, 1933, **55**, 2387). Jacober and Kraus (*loc. cit.*) claim a minimum in the case of aluminium bromide–methyl bromide, though this is not obvious from the data given.

It has been pointed out previously (Fairbrother, *J.*, 1941, 293; 1945, 503) that a review of the thermal energies involved and of other experimental data suggests that, although a rapid exchange of halogen atoms can take place between an aluminium and an organic halide, probably by an ionic mechanism, yet the proportion of organic halide molecules which are ionised at any one instant, even as undissociated ion-pairs, may be very small.

It is therefore pertinent to enquire to what extent this small observed conductivity is a result of the ionic dissociation of a binary complex involving the organic halide, and to what extent it is due to the ionisation of the aluminium bromide.

With this end in view, a number of transport experiments were carried out in the apparatus shown in Fig. 3. This was constructed of Pyrex glass and was totally enclosed without stopcocks, thus avoiding any possible contamination by lubricants. The cell was filled *in vacuo* in much the same manner as the conductivity cell, up to calibration marks on the electrode vessels, and was then sealed at *A*. The amount of current passed was measured by a copper voltameter in series with the electrolysis cell. At the conclusion of an experiment the anode and cathode compartments, *X* and *Y*, were separated by tilting the apparatus, whereby the connection between them was broken at *F*, as shown in the insets. Dry nitrogen was admitted, and the contents of *X* and *Y* were removed through tubes at the rear as shown in the side view at *S*.

With the object of diminishing the rate of decomposition of the solutions, the electrolyses were carried out at −78°. During the long time of electrolysis (8 hr.), however, some decomposition probably occurred and the results could only be considered as semi-quantitative. Nevertheless, they showed a net transport of aluminium to the cathode and of bromine to the anode, with the anion the predominant carrier.

Van Dyke (*J. Amer. Chem. Soc.*, 1950, **72**, 3619) came to somewhat similar conclusions from a study of the electrolysis of aluminium bromide in methyl bromide at −78°. He obtained liberation both of aluminium at the cathode and of bromine at the anode, and suggested that the ionic species responsible for the conduction were Br^- and $AlBr_2^+$.

In the present work we observed neither free bromine at the anode nor metallic aluminium at the cathode. The absence of free bromine in the anode compartment may be the result of its reaction with the unsaturated species present, since ethyl bromide solutions are much less stable than methyl bromide solutions, even at the same temperature. Any free Br^- ions would most certainly be attached to the strongly acceptor aluminium bromide molecules. The absence of metallic aluminium on the cathode and the somewhat greater mobility of the anion are best explained in this case, not by the formation of Br^- and $AlBr_2^+$, but of $AlBr_4^-$ and $C_2H_5BrAlBr_2^+$, of which the latter would break up at the cathode into aluminium bromide and discharged carbonium ion, or olefin and hydrogen ion.

Measurements of the rise of boiling point (Wertyporoch, *loc. cit.*) and of lowering of vapour pressure (Van Dyke, *loc. cit.*; Brown and Wallace, *loc. cit.*) all indicate that aluminium bromide is present in ethyl bromide solution essentially as a monomer, whilst Brown and Wallace's phase studies show that, at all events below 0°, it is present as a 1 : 1 complex. These results do not exclude the formation of small concentrations of the conducting species $AlBr_4^-$ and $C_2H_5BrAlBr_2^+$. It is clear, however, that the process responsible for the conduction is principally the dissociation of the aluminium bromide rather than of a simple electrolytic dissociation of an ion-pair $C_2H_5^+$ $AlBr_4^-$ which would give a transport of aluminium to the anode.

THE UNIVERSITY OF MANCHESTER. [*Received, September 20th*, 1954.]

β-*Aroylpropionic Acids. Part IV.* The Action of Grignard Reagents on Succinic Anhydride : β-Aroylpropionic Acids and their Esters.*

By F. G. Baddar, Lanson S. El-Assal, and (Miss) Adiba Habashi.

[Reprint Order No. 5035.]

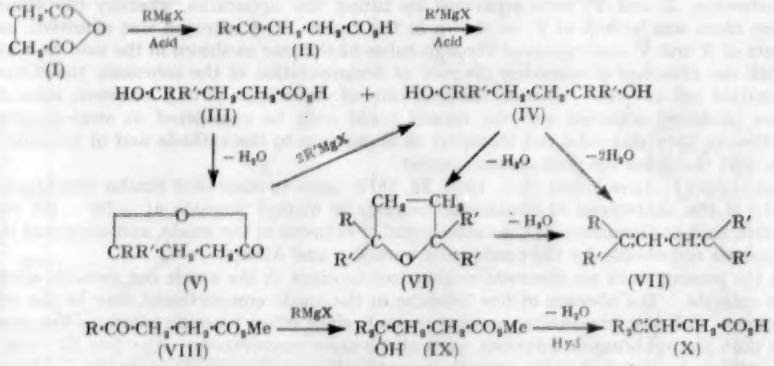
Arylmagnesium halides react with succinic anhydride (I) to give a mixture containing a β-aroylpropionic acid (II), a γγ-diaryl-γ-hydroxybutyric acid (III), and a neutral product from which a tetrahydrofuran (VI) or a buta-1 : 3-diene (VII) are isolated. The same products are obtained when succinic anhydride is replaced by the β-aroylpropionic acid corresponding to the Grignard reagent.

However, when arylmagnesium halides react with β-aroylpropionic esters, they give 3 : 3-diarylprop-2-ene-1-carboxylic acids instead of γγ-diaryl-γ-hydroxybutyric acids.

Identical lactones are obtained either by the interaction of R'MgX and $R{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ or of RMgX and $R'{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$.

Ethylmagnesium iodide reacts with β-aroylpropionic acids to give γ-aryl-γ-ethylbutyrolactones.

Baddar and El-Assal (Part II *) reported that, although reaction between succinic anhydride and *o*-methoxyphenylmagnesium bromide gave γγ-di-*o*-methoxyphenylbutyrolactone (V; $R = R' = o\text{-}MeO{\cdot}C_6H_4$), yet *p*-methoxyphenylmagnesium iodide afforded β-*p*-methoxybenzoylpropionic acid. Newman and Wise (*J. Amer. Chem. Soc.*, 1941, **63**, 2109) obtained similar results from the reaction between *o*-methoxyphenylmagnesium bromide or other arylmagnesium halides and naphthalic anhydride. We therefore studied the effect of the nature and the position of substituents on the course of this reaction.



When phenyl-, *p*-methoxyphenyl-, *o*-methoxyphenyl-, *o*-ethoxyphenyl-, or *o*-tolylmagnesium halide reacted with succinic anhydride, it gave a mixture of β-aroylpropionic acid (II), a γγ-diaryl-γ-hydroxybutyric acid (III) [isolated as its lactone (V)], and a neutral product from which a 2 : 2 : 5 : 5-tetra-aryltetrahydrofuran (VI) or a 1 : 1 : 4 : 4-tetra-arylbuta-1 : 3-diene (VII) were isolated. The same products were obtained when succinic anhydride was replaced by β-aroylpropionic acids. Lactones (V; $R = R' = Ph$, and $R = R' = o\text{-}MeO{\cdot}C_6H_4$) with the corresponding arylmagnesium halides gave 2 : 2 : 5 : 5-tetra-aryltetrahydrofurans (VI; $R = R' = Ph$, and $R = R' = o\text{-}MeO{\cdot}C_6H_4$, respectively). However, when β-aroylpropionic esters were used, 3 : 3-diarylprop-2-ene-1-carboxylic acids (X) were obtained. The reaction between β-aroylpropionic acids ($R{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$) and Grignard reagents (R'MgX) gave lactones (V) identical with those obtained from $R'{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ and RMgX. Ethylmagnesium halide reacted with β-benzoylpropionic and β-*o*-methoxybenzoylpropionic acid to give the lactones

* Parts II and III, *J.*, 1951, 431; 1954, 4538.

(V; R = Ph, R′ = Et) and (V; R = *o*-MeO·C_6H_4, R′ = Et), respectively, the latter in greater proportion. The above results are summarised in the Table.

Grignard reagent (2 mols.)	Reactant and subst.	Product, %,* of type: (II)	(V)	(VI)	(VII)	(X)
R = Ph	I	25·3	10·9—12·6	0·8	—	—
R′ = Ph	II; R = Ph	54 (r)	6·7	2·4	—	—
R′ = Ph (4 mols.)	V; R = R′ = Ph	—	—	2·9 (pure)	—	—
R = Ph	VIII; R = Ph	—	—	1·8 (pure)	—	24·2
R = *p*-MeO·C_6H_4	I	28·9	10·0	←2·1 (crude)→		—
R′ = "	II; *p*-MeO·C_6H_4	72 (r)	4·2	—	6·5 (pure)	—
R = "	VIII; "	—	—	←1·5→		18·6§
R = *o*-MeO·C_6H_4	I	18·8	25·2	1·2 (pure)	—	—
R′ = "	II; *o*-MeO·C_6H_4	23 (r)	28·0	8·4	—	—
R′ = " (4 mols.)	V; "	—	—	15·0	—	—
R = "	VIII; "	—	—	15·0	—	33·5
R = *o*-EtO·C_6H_4	I	15·8	7·6—9·2	2·7	—	—
R = *o*-Me·C_6H_4	I	18·2	6·4	†	†	—
R′ = Ph	II; *o*-MeO·C_6H_4	28 (r)	10·8	†	†	—
R′ = *o*-MeO·C_6H_4	II; Ph	35 (r)	10·9	5·3	—	—
R′ = "	II; *o*-EtO·C_6H_4	38 (r)	5·6	—	4·5	—
R′ = *o*-EtO·C_6H_4	II; *o*-MeO·C_6H_4	28 (r)	5·3	—	6·4	—
R′ = Et	II; Ph	35 (r)	9·3	‡	‡	—
R′ = Et	II; *o*-MeO·C_6H_4	25 (r)	18·3	‡	‡	—

* The yields are calculated on the crude product unless otherwise stated; (r) = recovered.

† The neutral portion was an oil which failed to solidify.

‡ The neutral products were mixtures which could not be adequately separated by fractional distillation.

§ When 4 mols. of the Grignard were used no propene acid was obtained, and the neutral portion gave 2·3% of (pure) butadiene and 0·9% of unidentified material.

The structure of the two buta-1 : 3-dienes (VII; R = *o*-EtO·C_6H_4, R′ = *o*-MeO·C_6H_4) and (VII; R = *o*-MeO·C_6H_4, R′ = *o*-EtO·C_6H_4) was confirmed by their absorption spectra being identical with that of 1 : 1 : 4 : 4-tetra-*p*-methoxyphenylbuta-1 : 3-diene (VII; R = R′ = *p*-MeO·C_6H_4) ($\lambda_{max.}$ = 335, 334, and 363 mμ, respectively), and different from that of the tetrahydrofurans (VI; R = R′ = Ph, R = R′ = *o*-MeO·C_6H_4, R = R′ = *o*-EtO·C_6H_4, and R = Ph, R′ = *o*-MeO·C_6H_4), which closely resemble that of diphenylmethane [$\lambda_{max.}$ = 259, 277, 274, 273(279), and 262 mμ, respectively]. The buta-1 : 3-diene (VII; R = R′ = Ph) exhibits $\lambda_{max.}$ at 343 mμ (Alberman *et al.*, *J.*, 1952, 3284).

The relatively high yield of the lactone obtained from the action of Grignard reagents on β-*o*-methoxybenzoylpropionic acid is therefore readily interpreted as explained by Baddar and El-Assal (*loc. cit.*). However, the exceptionally high yield of the lactone obtained from β-*o*-methoxybenzoylpropionic acid and *o*-methoxyphenylmagnesium halide may be due to the reactivity of the Grignard reagent caused by the co-ordination of the ethereal oxygen with the magnesium atom in the same molecule.

Experimental

The procedure described in the first experiment was adopted with slight modification in the remaining experiments.

Action of Phenylmagnesium Iodide on Succinic Anhydride, β-Benzoylpropionic Acid, Methyl β-Benzoylpropionate, and γγ-Diphenylbutyrolactone.—(i) An ethereal solution (40 ml.) of phenylmagnesium iodide (from iodobenzene; 20·4 g., 1 mol.) was added dropwise (20 min.) to a boiling solution of succinic anhydride (10 g., 1 mol.) in dry, thiophen-free benzene (200 ml.). The mixture was refluxed for a further 3 hr., left overnight at room temperature, and then treated with dilute sulphuric acid. The ether–benzene layer was extracted with sodium hydroxide solution, and the alkaline solution (charcoal) was cooled and acidified. The precipitated acids (*ca.* 5·4 g.) were refluxed with benzene for 1·5—2 hr., solvent was removed, and the semi-solid residue was extracted with cold sodium carbonate solution. The insoluble viscous oil (A) (*ca.* 0·6 g.) solidified on trituration with cold alcohol. On crystallisation from benzene–light petroleum (b. p. 40—60°), γγ-diphenylbutyrolactone was obtained, of m. p. 90·5—91·5° undepressed on admixture with an authentic specimen prepared by Stobbe's reaction (cf. Johnson *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 74) (Found: C, 80·0; H, 5·7%; *M*, 200. Calc. for $C_{16}H_{14}O_2$: C, 80·7; H, 5·9%; *M*, 238).

The sodium carbonate solution gave on acidification an acid (B) (*ca.* 4·2 g.), which on crystallisation from benzene–light petroleum (b. p. 40—60°) gave β-benzoylpropionic acid, m. p. and mixed m. p. 115—116°. The neutral product in the ether–benzene layer was refluxed for 1—2 hr. with 20% sodium hydroxide solution to remove any lactone. The insoluble semi-solid (C) was converted into a solid (D) (0·2 g.) on trituration with cold alcohol or extraction with hot light petroleum (b. p. 40—60°). It was refluxed with acetic acid for 1 hr., then allowed to crystallise, giving tetrahydro-2 : 2 : 5 : 5-tetraphenylfuran, m. p. 180° (Found : C, 88·4; H, 6·4%; *M*, 328. Calc. for $C_{28}H_{24}O$: C, 89·3; H, 6·4%; *M*, 376). Komppa and Rohrmann (*Annalen*, 1934, **509**, 259) and Valeur (*Compt. rend.*, 1903, **136**, 695) gave m. p. 180° and 182°, respectively. The experiment was repeated with β-benzoylpropionic acid and γγ-diphenylbutyrolactone, and the results are tabulated below :

		Products, g.		
PhMgX, mols.	Reactant (R = R′ = Ph)	Keto-acid (B) (II; R = Ph)	Lactone (A) (V; R = R′ = Ph)	Neutral (D) (R = R′ = Ph)
2	I (10 g.)	4·5	2·6—3·0	0·3
2	II (10 g.)	4·8 (r) *	0·9	0·5 †
3	V (2 g.)	—	—	0·8 ‡

* (r) = recovered.

† M. p. 150—155°, raised by repeated extraction with light petroleum (b. p. 40—60°) to 175—180°. On crystallisation from acetic acid two types of crystals were obtained, which were mechanically separated. The main product was recrystallised from the same solvent to give (VI; R = R′ = Ph), identified by m. p. and mixed m. p. The minor product (trace) melted at 210—225° and was not sufficient for identification.

‡ The reaction mixture was refluxed for 6 hr., and the neutral product (D) was proved to be the tetrahydrofuran (VI; R = R′ = Ph) by m. p. and mixed m. p. (Found : C, 88·8; H, 6·4%).

(ii) The reaction was repeated with phenylmagnesium iodide (2 mols.) and methyl β-benzoylpropionate (5 g.; 1 mol.). Acidification of the sodium hydroxide extract precipitated an acid (*ca.* 1·5 g.), which gave 3 : 3-diphenylprop-2-ene-1-carboxylic acid (X; R = Ph) (from dilute alcohol), m. p. 116—117°, depressed to 90° on admixture with β-benzoylpropionic acid (Found : C, 80·1; H, 5·7. Calc. for $C_{16}H_{14}O_2$: C, 80·7; H, 5·9%). Johnson *et al.* (*loc. cit.*) gave m. p. 117·5—118·5°. Oxidation with alkaline potassium permanganate afforded benzophenone (cf. Baddar and El-Assal, *loc. cit.*).

The viscous oil (C) was refluxed with 20% sodium hydroxide solution, then treated with alcohol. The alkaline solution, on acidification, precipitated β-benzoylpropionic acid (1·2 g.). The neutral portion (D) (0·2 g.), m. p. 198—200°, which was probably the diol (cf. Wassermann and Kloetzel, *J. Amer. Chem. Soc.*, 1953, **75**, 3037; Valeur, *loc. cit.*), gave tetrahydro-2 : 2 : 5 : 5-tetraphenylfuran (from glacial acetic acid), m. p. and mixed m. p. 180°.

Action of o-Methoxyphenylmagnesium Bromide on Succinic Anhydride, β-o-Methoxybenzoylpropionic Acid, and γγ-Di-o-methoxyphenylbutyrolactone.—(i) The Grignard reagent from *o*-bromoanisole (18·7 g., 1 mol.) was treated with succinic anhydride (10 g., 1 mol.) in the usual manner. The alkaline extract contained γγ-di-*o*-methoxyphenylbutyrolactone (A) (*ca.* 4·0 g.) and β-*o*-methoxybenzoylpropionic acid (B) (*ca.* 1·7 g.) (cf. Baddar and El-Assal, *loc. cit.*). The neutral, sticky solid (C) was triturated with alcohol, the product (D) (*ca.* 2·0 g.), m. p. 110—116°, extracted with hot acetone (30—40 ml.), and the insoluble fraction was filtered off (*ca.* 0·4 g.), m. p. 274—276°. Crystallisation from nitrobenzene gave *tetrahydro-2 : 2 : 5 : 5-tetra-o-methoxyphenylfuran* (VI; R = R′ = *o*-C_6H_4·OMe), m. p. 287·5—288·5° (Found : C, 77·8; H, 6·7; OMe, 22·6. $C_{32}H_{32}O_5$ requires C, 77·4; H, 6·45; OMe, 25·5%). The acetone solution on cooling deposited a crystalline product, m. p. 104—108° (cleared at 150°; *ca.* 1·0 g.), which could not be purified by fractional crystallisation. It gave no derivative with 2 : 4-dinitrophenylhydrazine. The experiment was repeated under varying conditions, and also with β-*o*-methoxybenzoylpropionic acid and the lactone (V; R = R′ = *o*-MeO·C_6H_4) instead of succinic anhydride. The results are given below :

o-MeO·C_6H_4·MgX, mols.	Reactant (10 g.) (R = R′ = *o*-MeO·C_6H_4)	Keto-acid (B), g.	Lactone (A), g.	Neutral (D) Wt. (g.) and m. p.
2	I	3·9	7·5	2·9, 110—116°
2 *	I	3·9	3·0	4·0, 110—116
2	II	2·3 ‡	4·0	2·0, 220—230
4 †	V	—	—	2·5, 250—260

* Refluxed for 5 hr. instead of 3 hr. † Refluxed for 6 hr. instead of 3 hr., and the product insoluble in ether–benzene was filtered off (*ca.* 1·5 g.), combined with (D) (*ca.* 1·0 g.), and purified as usual. ‡ Recovered.

Action of o-*Methoxyphenylmagnesium Bromide on Methyl* β-o-*Methoxybenzoylpropionate.*—The Grignard reagent (from *o*-bromoanisole; 10·2 g., 2 mols.) was added to a benzene solution (60 ml.) of methyl β-*o*-methoxybenzoylpropionate (6 g., 1 mol.), and the reaction mixture worked up. The insoluble product (*ca.* 2·0 g.) (D′) had m. p. 230—250°. The acid (2·7 g.) precipitated from the sodium hydroxide extract crystallised from benzene–light petroleum (b. p. 40—60°) to give 3 : 3-di-*o*-methoxyphenylprop-2-ene-1-carboxylic acid, identical (m. p. and mixed m. p.) with an authentic specimen (cf. Baddar and El-Assal, *loc. cit.*).

A mixture of solids (D) (*ca.* 0·5 g.), m. p. 230—240°, and (D′) was extracted with boiling acetone. The insoluble fraction (*ca.* 2·0 g.), m. p. 255—260°, crystallised from nitrobenzene to give tetrahydro-2 : 2 : 5 : 5-tetra-*o*-methoxyphenylfuran, m. p. and mixed m. p. 287·5—288·5°.

Action of o-*Ethoxyphenylmagnesium Iodide on Succinic Anhydride.*—The precipitate obtained on acidification of the product of the reaction of the Grignard reagent (from *o*-iodophenetole; 49·6 g., 2 mols.) and succinic anhydride (10 g., 1 mol.) was dissolved in hot sodium carbonate solution, the hot solution filtered, and the crystalline sodium salt obtained on cooling was treated with acid. *γγ-Di-o-ethoxyphenylbutyrolactone* (V; R = R′ = *o*-C_6H_4·OEt) (*ca.* 2·5—3 g.; m. p. 148—150°), formed monoclinic crystals, m. p. 157—157·5°, from acetic acid (Found: C, 73·6; H, 6·7; OEt, 28·6. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·7; OEt, 27·6%).

On acidification the sodium hydroxide extract precipitated β-*o-ethoxybenzoylpropionic acid* (needles from benzene), m. p. 123—124° undepressed on admixture with a specimen prepared from β-*o*-hydroxybenzoylpropionic acid ethyl iodide and potassium carbonate in dry acetone (Found: C, 64·6; H, 6·2; OEt, 21·05. $C_{13}H_{14}O_4$ requires C, 64·9; H, 6·3; OEt, 20·3%).

The neutral product (D) (1·5 g.) was repeatedly extracted with boiling light petroleum (b. p. 60—80°), refluxed with glacial acetic acid for 1 hr., and then dissolved in benzene, a little insoluble material being removed. The solution was diluted with light petroleum (b. p. 40—60°), to give 2 : 2 : 5 : 5-*tetra-o-ethoxyphenyltetrahydrofuran*, m. p. 207·5—208·5° (Found: C, 77·8; H, 7·3. $C_{36}H_{40}O_5$ requires C, 78·3; H, 7·3%).

Use of 1 mol. of the Grignard reagent gave yields of lactone, keto-acid, and neutral material of 3·5, 3·5, and 0·2 g., respectively.

Action of p-*Methoxyphenylmagnesium Bromide on Succinic Anhydride and on* β-p-*Methoxybenzoylpropionic Acid.*—(i) The product from the reaction of the Grignard reagent from *p*-bromoanisole (18·7 g., 1 mol.) and a solution of succinic anhydride (10 g., 1 mol.) in benzene (200 ml.) contained γγ-di-*p*-methoxyphenylbutyrolactone, m. p. and mixed m. p. 107·5—108·5° (from ether) (cf. Johnson *et al.*, *J. Amer. Chem. Soc.*, 1950, **72**, 513) (A) (0·8 g.), β-*p*-methoxybenzoylpropionic acid (B) (6·0 g.), and a neutral substance (D) (0·6 g.). A benzene solution of the neutral fraction (D) was passed on to alumina. Evaporation of the eluate obtained with benzene–ethyl acetate (1 : 1, vol.) and repeated crystallisation of the residue from benzene–light petroleum (b. p. 40—60°) gave 1 : 1 : 4 : 4-tetra-*p*-methoxyphenylbuta-1 : 3-diene, m. p. 203—204° undepressed by a specimen kindly supplied by Dr. Tadros (cf. Tadros *et al.*, *J.*, 1951, 2555) (Found: C, 80·6; H, 6·2; OMe, 23·0. Calc. for $C_{32}H_{30}O_4$: C, 80·3; H, 6·3; OMe, 25·9%).

(ii) With 2 mols. of the Grignard reagent, the yields of (A), (B), and (D) were 3·0, 6·0, and 1·0 g., respectively.

(iii) The Grignard reagent (18·0 g., 2 mols.) and β-*p*-methoxybenzoylpropionic acid (10 g., 1 mol.) gave a lactone (A) (0·6 g.), unchanged keto-acid (B) (7·2 g.), and 1 : 1 : 4 : 4-tetra-*p*-methoxyphenylbuta-1 : 3-diene (crude yield, 1·5 g.), m. p. and mixed m. p. 203—204°. The alcohol used in the trituration of the crude butadiene gave a trace of material identical with the specimen obtained by the action of Grignard reagent on the ester.

Action of p-*Methoxyphenylmagnesium Bromide on Methyl* β-p-*Methoxybenzoylpropionate.*—The Grignard reagent from *p*-bromoanisole (10·2 g., 2 mols.) was added to the ester (6 g., 1 mol.), and the reaction was carried out as usual. The semi-solid acid, after purification through the ester (1·5 g.) and crystallisation from light petroleum (b. p. 40—60°), gave 3 : 3-di-*p*-methoxyphenylprop-2-ene-1-carboxylic acid (X; R = R′ = *p*-C_6H_4·OMe), m. p. and mixed m. p. 86—87° (cf. Johnson *et al.*, *loc. cit.*). The neutral product (D) (*ca.* 0·2 g.), m. p. 190—222°, was not identified.

With 4 mols. of the Grignard reagent, no propene-acid was obtained. The neutral viscous oil (C) gave unidentified material (crude yield, 0·2 g.), m. p. 213—214°, and 1 : 1 : 4 : 4-tetra-*p*-methoxyphenylbuta-1 : 3-diene (crude yield, 0·5 g.), yellow crystals, m. p. 203—204° (from benzene–light petroleum).

Action of o-*Tolylmagnesium Iodide on Succinic Anhydride.*—The reaction between *o*-tolylmagnesium iodide (from *o*-iodotoluene; 21·8 g., 1 mol.) and succinic anhydride (10 g., 1 mol.)

gave *γγ-di-o-tolylbutyrolactone* (A) (V; R = R′ = *o*-C_6H_4Me) (crude yield, 0·5 g.), m. p. 138—139° (from light petroleum) (Found: C, 81·0; H, 6·8%; *M*, 248. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%; *M*, 266), β-*o-toluoylpropionic acid* (B) (crude yield, 3·5 g.), m. p. 104—105° (from benzene–light petroleum) (Found: C, 68·5; H, 6·1. $C_{11}H_{12}O_3$ requires C, 68·6; H, 6·3%), and a neutral portion (C) (1·4 g.) which failed to solidify and did not give a solid nitro-derivative.

When 2 mols. of the Grignard reagent were used, the amounts of the lactone (A), keto-acid (B), and neutral product (C) were 1·7, 3·5, and 3·0 g., respectively.

Action of o-*Methoxyphenylmagnesium Iodide on* β-*Benzoylpropionic Acid.*—The Grignard reagent (from *o*-iodoanisole; 26·4 g., 2 mols.) and a benzene solution (100 ml.) of β-benzoylpropionic acid (10 g., 1 mol.) gave crude *o-methoxy-γγ-diphenylbutyrolactone* (A) (V; R = Ph; R′ = *o*-C_6H_4·OMe) (*ca.* 1·8 g.), unchanged keto-acid (B) (3·5 g.), and a neutral product (D). The pure lactone (*ca.* 0·3 g.) had m. p. 73—74° [Found: C, 76·5; H, 5·9; OMe, 11·9%; *M* (Rast), 240. $C_{17}H_{16}O_3$ requires C, 76·1; H, 5·9; OMe, 11·5%; *M*, 268]. The neutral solid (D) (*ca.* 1·4 g.), m. p. 170—175° (clearing at 190°), was crystallised from glacial acetic acid, and the first crop, m. p. 200—204°, was recrystallised from the same solvent giving 2 : 2 : 5-*tri*-o-*methoxyphenyl-5-phenyltetrahydrofuran* (VI; R = C_6H_5, R′ = *o*-C_6H_4·OMe), m. p. 208—209° (Found: C, 80·1; H, 6·6; OMe, 18·8%; *M*, 470. $C_{31}H_{30}O_4$ requires C, 79·8; H, 6·4; OMe, 19·8%; *M*, 466). The second crop, m. p. 135—140° (cleared at 190°), could not be purified by fractional crystallisation. It failed to give either the unsaturation test (bromine) or a 2 : 4-dinitrophenylhydrazone.

Action of Phenylmagnesium Iodide on β-o-*Methoxybenzoylpropionic Acid.*—The reaction between phenylmagnesium iodide (from iodobenzene; 15·8 g., 2 mols.) and β-*o*-methoxybenzoylpropionic acid (8 g.; 1 mol.) gave *o*-methoxy-γγ-diphenylbutyrolactone (A) (crude yield, (1·1 g.), m. p. and mixed m. p. 73—74°, unchanged keto-acid (B) (2·2 g.), and a neutral portion (C) (*ca.* 1·0 g.). Fraction (C) remained liquid and was not identified.

Action of o-*Ethoxyphenylmagnesium Iodide on* β-o-*Methoxybenzoylpropionic Acid.*—The reaction between the Grignard reagent from *o*-iodophenetole (19·2 g., 2 mols.) and the keto-acid (8 g., 1 mol.) was carried out as usual. The neutral product (D′), precipitated on decomposition of the Grignard complex, was worked up with the remainder of (D) (see below). The viscous oily lactone (0·6 g.) after trituration with ether and crystallisation from methyl alcohol gave *o-ethoxy-o′-methoxy-γγ-diphenylbutyrolactone* (V; R = *o*-C_6H_4·OMe, R′ = *o*-C_6H_4·OEt), m. p. 122—123° (Found: C, 72·9; H, 6·4. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4%).

The combined neutral product (D + D′) (*ca.* 0·5 g.) was boiled with 20% sodium hydroxide solution, and then crystallised from glacial acetic acid, giving 1 : 1 : 4-*tri*-o-*ethoxyphenyl*-4-o-*methoxyphenylbuta*-1 : 3-*diene* (VII; R = *o*-C_6H_4·OMe, R′ = *o*-C_6H_4·OEt), m. p. 195—196° (Found: C, 80·7; H, 6·8%; *M*, 601. $C_{38}H_{38}O_4$ requires C, 80·8; H, 6·9%; *M*, 520).

Action of o-*Methoxyphenylmagnesium Bromide on* β-o-*Ethoxybenzoylpropionic Acid.*—The Grignard reagent from *o*-bromoanisole (6·72 g., 2 mols.) and β-*o*-ethoxybenzoylpropionic acid (4 g., 1 mol.) gave a neutral portion (D) (*ca.* 0·4 g.) and *o*-ethoxy-*o′*-methoxy-γγ-diphenylbutyrolactone (crude yield, 0·3 g.), m. p. 122—123°, undepressed on admixture with an authentic specimen from the preceding experiment.

An acetone solution of solid (D), on cooling, deposited 4-o-*ethoxyphenyl*-1 : 1 : 4-*tri*-o-*methoxyphenylbuta*-1 : 3-*diene* (VII; R = *o*-C_6H_4·OEt, R′ = *o*-C_6H_4·OMe), m. p. 188—189° (after crystallisation from acetic acid) (Found: C, 80·4; H, 6·5. $C_{33}H_{32}O_4$ requires C, 80·5; H, 6·5%).

Action of Ethylmagnesium Iodide on β-*Benzoyl- and on* β-o-*Methoxybenzoyl-propionic Acid.*—(i) Reaction between ethylmagnesium iodide (from ethyl iodide; 17·5 g., 2 mols.) and β-benzoylpropionic acid (10 g., 1 mol.) gave γ-ethyl-γ-phenylbutyrolactone (A) (*ca.* 1·0 g.), unchanged keto-acid (B) (*ca.* 3·5 g.), and a neutral oil (*ca.* 1·4 g.) (C). The lactone (A) was a faintly yellow oil, b. p. 135—138°/2 mm., n_D^{27} 1·5250 (Found: C, 75·4; H, 7·4. Calc. for $C_{12}H_{14}O_2$: C, 75·8; H, 7·4%). Johnson *et al.* (*J. Amer. Chem. Soc.*, 1947, **69**, 74) gave b. p. 135°/0·05 mm., n_D^{20} 1·5283. (ii) A similar experiment with ethylmagnesium iodide (from ethyl iodide; 12·0 g., 2 mols.) and β-*o*-methoxybenzoylpropionic acid (8·0 g., 1 mol.) gave *γ-ethyl-γ-o-methoxyphenylbutyrolactone* (crude yield, 1·5 g.), b. p. 155—158°/4 mm., n_D^{27} 1·5725 (Found: C, 70·8; H, 7·2; OMe, 14·6. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3; OMe, 14·1%), unchanged keto-acid (about 2·0 g.), and an oil (C) (about 1·3 g.) which was not identified.

The identification of all the constituents of the neutral mixtures in the above reactions is now in progress.

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Phenylpropiolic Acids. Part IV. The Self-condensation of* o- *and* p-*Tolyl- and* o-*Chlorophenyl-propiolic Acids.*

By F. G. Baddar, Lanson S. El-Assal, and Naguib A. Doss.

[Reprint Order No. 5411.]

o- and *p*-Tolylpropiolic acids are converted by acetic anhydride into 7-methyl-1-*p*-tolyl- and 5-methyl-1-*o*-tolyl-naphthalene-2 : 3-dicarboxylic anhydride, identical with the cyclisation products from di-*p*-methyl- and di-*o*-methyl-benzylidenesuccinic anhydride, respectively. The first two anhydrides are converted by aluminium chloride into 3′ : 7- and 1′ : 5-dimethyl-3 : 4-benzofluorenone-1-carboxylic acid, respectively, and the former acid is decarboxylated to 3′ : 7-dimethyl-3 : 4-benzofluorenone. Fusion of the 3′ : 7-dimethyl-acid with potassium hydroxide gives 7-methyl-1-(2-carboxy-*p*-tolyl)naphthalene-3-carboxylic acid and a trace of the 2 : 3-dicarboxylic acid. Concentrated sulphuric acid converts the former into 6 : 9-dimethyl*meso*benzanthrone-2-carboxylic acid which is decarboxylated to 6 : 9-dimethyl-*meso*benzanthrone.

o-Chlorophenylpropiolic acid, when similarly treated, gives 5-chloro-1-*o*-chlorophenylnaphthalene-2 : 3-dicarboxylic anhydride. However, di-*o*-chlorobenzylidenesuccinic anhydride fails to cyclise to the corresponding anhydride.

In Parts I, II, and III (*J.*, 1947, 224; 1948, 1267; 1951, 1844) it was shown that phenylpropiolic acids were converted by acetic anhydride into the corresponding 1-phenylnaphthalene derivatives. The present investigation deals with other *o*- and *p*-substituted phenylpropiolic acids where the substituent is an electron-repelling or -attracting group.

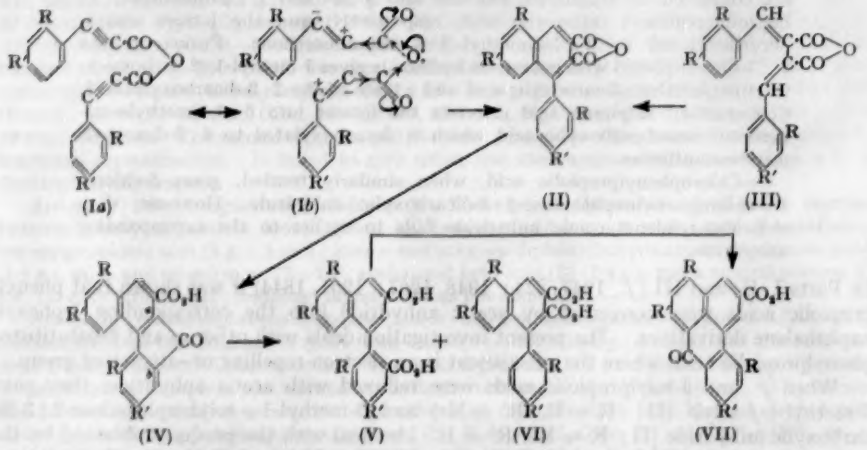
When *p*- and *o*-tolylpropiolic acids were refluxed with acetic anhydride, they gave 7-methyl-1-*p*-tolyl- (II; R = H, R′ = Me) and 5-methyl-1-*o*-tolylnaphthalene-2 : 3-dicarboxylic anhydride (II; R = Me, R′ = H), identical with the products obtained by the action of sunlight on di-4-methyl- (III; R = H, R′ = Me) and di-2-methyl-benzylidenesuccinic anhydride (III; R = Me, R′ = H), respectively. Both anhydrides were converted by aluminium chloride in nitrobenzene into 3′ : 7- (IV; R = H, R′ = Me) and 1′ : 5-dimethyl-3 : 4-benzofluorenone-1-carboxylic acid (IV; R = Me, R′ = H), respectively. The former acid was decarboxylated with copper-bronze in quinoline to 3′ : 7-dimethyl-3 : 4-benzofluorenone, and when fused with potassium hydroxide gave 7-methyl-1-(2-carboxy-*p*-tolyl)naphthalene-3-carboxylic acid (V; R = H, R′ = Me) together with a trace of the isomeric acid (VI; R = H, R′ = Me). This result agrees with Baddar and Gindy's view (*J.*, 1944, 450; 1948, 1231) that the factors determining the point of cleavage of 3 : 4-benzofluorenones are of polar origin, depending on the electron density at carbon atoms (*a*) and (*b*). The acid (V; R = H, R′ = Me) was cyclised by 90% sulphuric acid (cf. Baddar, *J.*, 1941, 310) to 6 : 9-dimethyl*meso*benzanthrone-2-carboxylic acid (VII; R = H, R′ = Me); the formation of a trace of 3′ : 7-dimethyl-3 : 4-benzofluorenone-1-carboxylic acid (IV; R = H, R′ = Me) could not be completely excluded (cf. Baddar, *loc. cit.*).

Fusion of either 7-methyl-1-*p*-tolylnaphthalene-2 : 3-dicarboxylic anhydride (II; R = H, R′ = Me) or 3′ : 7-dimethyl-3 : 4-benzofluorenone-1-carboxylic acid (IV; R = H, R′ = Me) with aluminium chloride–sodium chloride (cf. Baddar, *loc. cit.*) gave a mixture of isomeric *meso*benzanthronecarboxylic acids from which no pure product could be isolated—it is possible that the methyl group migrates under the influence of aluminium chloride.

5-Chloro-1-*o*-chlorophenylnaphthalene-2 : 3-dicarboxylic anhydride (II; R = Cl, R′ = H) was obtained either (*a*) by heating *o*-chlorophenylpropiolic acid with acetic anhydride, or (*b*) by refluxing *o*-chlorophenylpropioloyl chloride with *o*-chlorophenylpropiolic acid in benzene (cf. Baddar and El-Assal, Part III). However, the structure of the anhydride

* Part III, *J.*, 1951, 1844.

was established by the following facts: (i) It was insoluble in sodium carbonate solution but readily dissolved in boiling sodium hydroxide solution; the precipitated dibasic acid was converted back into the original anhydride when boiled with acetic anhydride, which indicated that it is an *o*-dibasic acid. (ii) Its solution in sodium hydrogen carbonate failed to discharge the colour of potassium permanganate solution, excluding the *cyclo*butadiene structure (cf. Baddar and El-Assal, Parts I—III). Attempted conversion of the anhydride (II; R = Cl, R′ = H) into the corresponding 3 : 4-benzofluorenone derivative (IV; R = Cl, R′ = H) by means of aluminium chloride in nitrobenzene either cold or at 150° was unsuccessful, probably owing to deactivation of the 6′-position of the phenyl group by the (−*I*) effect of the chlorine atom in the 2′-position.



o-Chlorobenzaldehyde was condensed with diethyl succinate to give di-2-chlorobenzylidenesuccinic acid. Its anhydride (III; R = Cl, R′ = H) gave, at 300° or on exposure of its benzene solution to sunlight, a mixture of products from which no pure 5-chloro-1-*o*-chlorophenylnaphthalene-2 : 3-dicarboxylic anhydride (II; R = Cl, R′ = H) could be isolated.

Attempted reaction of *o*-nitrophenylpropiolic acid under similar conditions gave an uncrystallisable material (see following paper).

Experimental

p- *and* o-*Methylcinnamic Acids*.—These were prepared from the corresponding tolualdehydes and malonic acid (Walling and Wolfstirn, *J. Amer. Chem. Soc.*, 1947, **69**, 852) in 60—70% yield. From ethanol or benzene, both acids crystallised in shining crystals, with respective m. p.s 199—200° (Stoermer, Grium, and Leage, *Ber.*, 1917, **50**, 979, gave m. p. 198—199°) and 175—176° (Auwers, *Annalen*, 1917, **413**, 265, gave 174—175°).

αβ-*Dibromo*-β-p-*tolylpropionic Acid*.—This was prepared as described by Gattermann (*Annalen*, 1906, **347**, 358), but with use of chloroform instead of carbon disulphide, in 70% yield; m. p. 193—194° (Gattermann gave m. p. 192°).

αβ-*Dibromo*-β-o-*tolylpropionic Acid*.—Similarly prepared from *o*-methylcinnamic acid (12 g.) and bromine (4 ml.) in carbon tetrachloride (100 ml.), and crystallised from benzene–light petroleum (b. p. 40—60°), this *acid* (70%) had m. p. 162—163° (Found: C, 37·7; H, 2·9; Br, 51·5. $C_{10}H_{10}O_2Br_2$ requires C, 37·3; H, 3·1; Br, 49·7%).

αβ-*Dibromo*-β-o-*chlorophenylpropionic Acid*.—This was prepared from *o*-chlorocinnamic acid (Stoermer, *Ber.*, 1911, **44**, 659) (5 g.) and bromine (1·5 ml.) in hot glacial acetic acid (50 ml.), and crystallised from benzene–light petroleum (b. p. 40—60°); it had m. p. 184—185° (*ca.* 8·5 g.) (Stoermer gave m. p. 184°) (Found: C, 31·8; H, 2·1; Hal., 57·0. Calc. for $C_9H_7O_2ClBr_2$: C, 31·5; H = 2·1; Hal., 57·0%).

Arylpropiolic Acids.—The following acids were prepared from the corresponding αβ-dibromophenylpropionic acids exactly as described by Reimer (*J. Amer. Chem. Soc.*, 1942, **64**, 2510) for phenylpropiolic acid: *p*-Tolylpropiolic acid, needles (from benzene), m. p. 149—150°; Gattermann (*loc. cit.*) gave m. p. 148—149° (95%). *o-Tolylpropiolic acid*, light-brown aggregates, m. p. 94—95° (95%) [from benzene–light petroleum (b. p. 60—80°)] (Found: C, 74·7; H, 5·1. $C_{10}H_8O_2$ requires C, 75·0; H, 5·0%). Attempted preparation of this acid by the method of *Org. Synth.*, 1932, **12**, 60, gave a poor yield of an impure product which was difficult to purify. *o*-Chlorophenylpropiolic acid (93%) crystallised from benzene in aggregates, m. p. 132—133° (decomp.) (Found: C, 59·6; H, 2·6; Cl, 19·4. Calc. for $C_9H_5O_2Cl$: C, 59·8; H, 2·9; Cl, 19·4%); Otto (*J. Amer. Chem. Soc.*, 1934, **56**, 1393) gave m. p. 131—132°. The acid *chloride*, b. p. 120—125°/1 mm., was a pale yellow liquid which solidified on cooling at 0° (Found: Cl, 37·0. $C_9H_4OCl_2$ requires Cl, 35·0%).

7-Methyl-1-p-tolylnaphthalene-2 : 3-dicarboxylic Anhydride (II; R = H, R′ = Me).—*p*-Tolylpropiolic acid (5 g.) was refluxed with acetic anhydride (12 ml.) for 4—5 hr., cooled, and diluted with ether; the precipitated anhydride was filtered off, m. p. 268—269° (*ca.* 4 g.), and crystallised from benzene–light petroleum (b. p. 40—60°) in pale yellow, shining crystals, m. p. and mixed m. p. 268—269°; Baddar, El-Assal, and Gindy (*J.*, 1948, 1272) gave m. p. 266—267°. The *dimethyl ester*, prepared by diazomethane and crystallised from methyl alcohol, had m. p. 140—141° (Found: C, 75·6; H, 5·6. $C_{22}H_{20}O_4$ requires C, 75·8; H, 5·7%).

3′ : 7-Dimethyl-3 : 4-benzofluorenone-1-carboxylic Acid (IV; R = H, R′ = Me).—A powdered mixture of the above anhydride (II; R = H, R′ = Me) (3 g.) and aluminium chloride (15 g.) was gradually added (30 min.) to stirred nitrobenzene (35 ml.), the temperature being kept below 50°. The mixture was then heated on a boiling-water bath for a further 6 hr. The product was hydrolysed as usual, nitrobenzene was removed with steam, the precipitated dark-brown product was filtered off and treated with ammonia, and the insoluble orange ammonium salt was filtered off and acidified. The liberated deep red acid was crystallised from xylene or benzene, giving *3′ : 7-dimethyl-3 : 4-benzofluorenone-1-carboxylic acid* in red needles, m. p. 292—293° (*ca.* 2·9 g.) (Found: C, 79·2; H, 4·9. $C_{20}H_{14}O_3$ requires C, 79·4; H, 4·7%). Its *methyl ester*, prepared with diazomethane in ether–dioxan, crystallised from benzene–light petroleum (b. p. 40—60°) in fine orange needles (84% yield), m. p. 224—225° (Found: C, 80·3; H, 5·1. $C_{21}H_{16}O_3$ requires C, 79·7; H, 5·1%).

3′ : 7-Dimethyl-3 : 4-benzofluorenone.—The acid (IV; R = H, R′ = Me) (0·5 g.) was decarboxylated by heating the stirred mixture with copper-bronze (0·06 g.) in quinoline (15 ml.) for 2 hr. at 205—210°. The *3′ : 7-dimethyl-3 : 4-benzofluorenone* crystallised from methyl alcohol in orange prismatic crystals, m. p. 145—146° (Found: C, 87·7; H, 5·4. $C_{19}H_{14}O$ requires C, 88·3; H, 5·4%); yield *ca.* 0·3 g.

7-Methyl-1-(2-carboxy-p-tolyl)naphthalene-3-carboxylic Acid (V; R = H, R′ = Me).—The acid (IV; R = H, R′ = Me) (1 g.) was heated with molten potassium hydroxide (7 g.) for 30 min. at 230—240° and worked up as usual (cf. Baddar and Gindy, *J.*, 1948, 1231). The product, m. p. 312—313° (1 g.), was refluxed with acetyl chloride for 30 min., acetyl chloride removed, ether added, and the insoluble 7-methyl-1-*p*-tolylnaphthalene-2 : 3-dicarboxylic anhydride (II; R = H, R′ = Me) filtered off (trace; identified by m. p. and mixed m. p.). The residue left on distillation of ether crystallised from acetic acid, giving *7-methyl-1-(2-carboxy-p-tolyl)naphthalene-3-carboxylic acid* (V; R = H, R′ = Me), m. p. 325—326° (Found: C, 75·1; H, 4·9. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%).

6 : 9-Dimethylmesobenzanthrone-2-carboxylic acid (VII; R = H, R′ = Me).—A mixture of the acid (V; R = H, R′ = Me) (1 g.) and cold concentrated sulphuric acid (5 ml.) was kept at 20—25° for 3 days. The solution was added to crushed ice, and the precipitated yellow product (*ca.* 0·95 g.) was crystallised from nitrobenzene, giving *6 : 9-dimethylmesobenzanthrone-2-carboxylic acid* in yellow crystals, m. p. >350° (Found: C, 79·4; H, 4·7. $C_{20}H_{14}O_3$ requires C, 79·4; H, 4·7%). Its *methyl ester*, prepared from diazomethane in ether–dioxan, crystallised from methyl alcohol in pale yellow prismatic needles, m. p. 218—219° (Found: C, 79·7; H, 4·8. $C_{21}H_{16}O_3$ requires C, 79·7; H, 5·0%).

6 : 9-Dimethylmesobenzanthrone.—The acid (VII; R = H, R′ = Me) (1 g.) was decarboxylated with copper-bronze (0·08 g.) and quinoline (5 ml.); *6 : 9-dimethylmesobenzanthrone* was obtained in orange needles (*ca.* 0·3 g.), m. p. 114—115° (from methanol) (Found: C, 87·8; H, 5·4. $C_{19}H_{14}O$ requires C, 88·3; H, 5·4%).

Fusion of 3′ : 7-Dimethyl-3 : 4-benzofluorenone-1-carboxylic Acid (IV; R = H, R′ = Me) *with Aluminium Chloride–Sodium Chloride.*—The acid (0·5 g.) was added to a stirred molten mixture of aluminium chloride (5 g.) and sodium chloride (1 g.) at 140—150° (oil-bath) and

kept thereat for 2·5 hr. The product was decomposed with dilute hydrochloric acid, filtered off, and extracted with ammonia, and the extract (charcoal) acidified. The precipitated *meso*-benzanthronecarboxylic acid mixture, crystallised from nitrobenzene, had m. p. >350°; esterification gave two fractions, m. p.s 195—205° and 205—212°. Fractional crystallisation failed to resolve the mixture.

Di-2-methylbenzylidenesuccinic Acid.—A mixture of diethyl succinate (8·7 g.; 1 mol.) and *o*-tolualdehyde (12 g.; 2 mol.) in dry ether (30 ml.) was quickly added to a stirred suspension of powdered, freshly prepared, alcohol-free sodium ethoxide (6·8 g.; 2 mol.) in dry ether (50 ml.) cooled at −15° to −18°. The mixture was kept below 0° for 4 days and then at 20—25° for several hours with occasional stirring, then worked up as usual (cf. Baddar, El-Assal, and Gindy, *J.*, 1948, 1270). The product crystallised from glacial acetic acid to give *di-2-methylbenzylidenesuccinic acid*, m. p. 223—224° (Found: C, 74·1; H, 5·7. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%); yield *ca.* 4 g. The *dimethyl ester* (diazomethane in ether–dioxan) formed needles, m. p. 105—107° (from methyl alcohol) (Found: C, 75·2; H, 6·0. $C_{22}H_{22}O_4$ requires C, 75·75; H, 6·4%).

Di-2-methylbenzylidenesuccinic Anhydride (III; R = Me, R′ = H).—A suspension of the above acid (0·5 g.) in acetyl chloride (3 ml.) was refluxed till it dissolved, then acetyl chloride was distilled off and the residue triturated with ether, filtered off, and dried (*ca.* 0·4 g.). The *anhydride* was obtained in monoclinic, lemon-yellow crystals, m. p. 154—155° [from benzene–light petroleum (b. p. 50—60°)] (Found: C, 79·3; H, 5·1. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%).

5-Methyl-1-o-tolylnaphthalene-2 : 3-dicarboxylic Anhydride (II; R = Me, R′ = H).—(*a*) A solution of the anhydride (III; R = Me, R′ = H) (0·5 g.) in benzene (5 ml.) and a tiny crystal of iodine were left in sunlight for 12 days (November) in a Pyrex tube. Distillation of the benzene left a residue which was heated in a vacuum at 100° for 2 hr. Repeated crystallisation from benzene–light petroleum (b. p. 50—60°) gave *5-methyl-1-o-tolylnaphthalene-2 : 3-dicarboxylic anhydride* in pale yellow needles, m. p. 162—163°, depressed to 110—120° on admixture with the original anhydride (II; R = Me, R′ = H) (Found: C, 79·6; H, 4·7. $C_{20}H_{14}O_3$ requires C, 79·4; H, 4·7%). (*b*) *o*-Tolylpropiolic acid (5 g.) was refluxed with acetic anhydride (10 ml.) for 4—5 hr., acetic anhydride was then evaporated off (reduced pressure), and the residue treated with ether, filtered off, washed, and dried; it had m. p. 160—161° (*ca.* 2·5 g.). 5-Methyl-1-*o*-tolylnaphthalene-2 : 3-dicarboxylic anhydride formed pale yellow needles, m. p. and mixed m. p. 162—163° [from benzene–light petroleum (b. p. 50—60°)] (Found: C, 78·9; H, 4·8%).

1′ : 5-Dimethyl-3 : 4-benzofluorenone-1-carboxylic Acid (IV; R = Me, R′ = H).—Powdered anhydride (II; R = Me, R′ = H) (0·5 g.) and aluminium chloride (2·5 g.) were added portionwise to stirred nitrobenzene (6 ml.), and the temperature was allowed to rise to 50—60° and kept thereat for a further 10 hr., and the product worked up as usual. It was digested with ammonia solution, and the extract filtered and acidified. The precipitate (0·45 g.) gave *1′ : 5-dimethyl-3 : 4-benzofluorenone-1-carboxylic acid* in deep red needles, m. p. 236—237° (from benzene) (Found: C, 78·9; H, 4·7. $C_{20}H_{14}O_3$ requires C, 79·7; H, 4·7%).

5-Chloro-1-o-chlorophenylnaphthalene-2 : 3-dicarboxylic Anhydride (II; R = Cl, R′ = H).—(*a*) *o*-Chlorophenylpropiolic acid (5 g.) was refluxed with acetic anhydride (20 ml.) for 6 hr., and then worked up as usual. The resulting *anhydride* (*ca.* 3 g.) crystallised from benzene–light petroleum (b. p. 40—60°) in needles, m. p. 193—194° (Found: C, 62·8; H, 2·3; Cl, 18·3. $C_{18}H_8O_3Cl_2$ requires C, 62·9; H, 2·3; Cl, 17·7%). (*b*) A mixture of *o*-chlorophenylpropiolic acid (1·0 g.) and its acid chloride (0·9 g.) in benzene (20 ml.) was refluxed for 30 hr. The benzene was distilled off, the residue treated with ether, and the insoluble product filtered off and dried, m. p. 186—188° (*ca.* 0·8 g.). On crystallisation as before, the anhydride formed needles, m. p. and mixed m. p. 193—194°. Its dibasic acid (0·5 g.) was esterified with diazomethane in ether; the *dimethyl ester* had m. p. 153—154° (from methyl alcohol) (Found: C, 62·1; H, 3·6; Cl, 17·6. $C_{20}H_{14}O_4Cl_2$ requires C, 61·6; H, 3·6; Cl, 18·2%).

When a finely powdered mixture of the anhydride (II; R = Cl, R′ = H) (2 g.) and ammonium carbonate (12·0 g.) was heated for an hour at 200—210°, the product was extracted with warm sodium hydroxide solution, the alkaline extract (charcoal) acidified, and the precipitate crystallised from glacial acetic acid, the *imide* was obtained in yellow needles, m. p. 218—219° depressed to 165—170° on admixture with the original anhydride (Found: C, 63·0; H, 2·3; Cl, 20·8; N, 4·0. $C_{18}H_9O_2NCl_2$ requires C, 63·1; H, 2·6; Cl, 20·8; N, 4·1%).

Di-2-chlorobenzylidenesuccinic Acid.—A solution of diethyl succinate (8 g.) and *o*-chlorobenzaldehyde (12·5 g.) in dry ether (30 ml.) was quickly added to a stirred suspension of dry, alcohol-free sodium ethoxide (3·5 g.) in dry ether (50 ml.) cooled at −15° to −18°, and the reaction completed as before. The mixture was shaken with cold water, and the ether layer

separated from the aqueous alkaline layer (*A*). Distillation of the ether left a residue which was hydrolysed with 20% sodium hydroxide solution. The insoluble neutral product in the alkaline solution (*B*) was re-extracted with ether, and the ethereal solution washed and dried (Na_2SO_4). Distillation of ether left a pale yellow oil which slowly solidified and crystallised from ethyl alcohol to give *o*-chlorobenzyl alcohol, needles, m. p. and mixed m. p. 71—72° (cf. Carothers and Adams, *J. Amer. Chem. Soc.*, 1924, **46**, 1681).

Acidification of the aqueous alkaline solution (*B*) (charcoal) precipitated an acid which was filtered off, washed, and dried, m. p. 125—126° (*ca.* 1 g.). This on two crystallisations from benzene gave needles, m. p. 130—131° depressed to 112—117° on admixture with *o*-chlorobenzoic acid. The structure of this acid is under investigation.

The alkaline solution (*A*) (charcoal) was refluxed for an hour till hydrolysis was complete and then worked up as usual (cf. Baddar and El-Assal, *loc. cit.*). The acid product was treated several times with hot benzene, and the insoluble product filtered off and crystallised from glacial acetic acid to give *di-2-chlorobenzylidenesuccinic acid*, m. p. 233—234° (Found: C, 59·1; H, 3·2; Cl, 19·4. $C_{18}H_{12}O_4Cl_2$ requires C, 59·5; H, 3·3; Cl, 19·5%); yield *ca.* 3 g. When the benzene mother-liquor evaporated slowly, it gave a few crystals embedded in a viscous oil. Those were mechanically separated and crystallised from the same solvent, forming needles, m. p. 130—131°, identical with the above unidentified product.

Di-2-chlorobenzylidenesuccinic Anhydride (III; R = Cl, R′ = H).—Prepared as usual and repeatedly crystallised from benzene–light petroleum (b. p. 40—60°), this *anhydride* formed lemon-yellow crystals, m. p. 184—185° (80%), (Found: C, 62·5; H, 2·9; Cl, 20·2. $C_{18}H_{10}O_3Cl_2$ requires C, 62·6; H, 2·9; Cl, 20·5%).

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Phenylpropiolic Acids. Part V. Self-condensation of* m-*Alkoxy- and* 3 : 4-*Dialkoxy-phenylpropiolic Acids.*

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[Reprint Order No. 5412.]

m-Alkoxyphenylpropiolic acids are converted by acetic anhydride into a mixture of colourless 6- and yellow 8-alkoxy-1-*m*-alkoxyphenylnaphthalene-2 : 3-dicarboxylic anhydride in equal amounts. The dibasic acids derived from the 3′ : 6-dialkoxy-anhydrides (II; R = Me or Et, R′ = H) are decarboxylated to 6-alkoxy-1-*m*-alkoxyphenylnaphthalenes.

The structure of the yellow anhydrides (III; R = Me and Et, R′ = H) follows from the fact that they give acid imides, and their alkaline solutions do not discharge the colour of potassium permanganate solution.

3 : 4-Diethoxyphenylpropiolic acid gives under the same conditions 6 : 7-diethoxy-1-(3′ : 4′-diethoxyphenyl)naphthalene-2 : 3-dicarboxylic anhydride together with a small amount of the 7 : 8-diethoxy-isomer. 3 : 4-Dimethoxyphenylpropiolic acid gives a mixture from which 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)naphthalene-2 : 3-dicarboxylic anhydride is the only isomer isolated in a pure state.

Cyclisation of *m*-substituted phenylpropiolic acids *via* the anhydrides (I) to 1-phenylnaphthalene derivatives could take place in either of two positions to give two isomeric compounds. We set out to test this assumption since Haworth and Sheldrick (*J.*, 1935, 636) and Haworth and Kelly (*J.*, 1936, 745) reported that they isolated from the action of acetic anhydride on 3 : 4-dimethoxy- and 3 : 4-methylenedioxy-phenylpropiolic acid only one 1-phenylnaphthalene-2 : 3-dicarboxylic anhydride.

m-Methoxyphenylpropiolic acid and acetic anhydride gave a mixture from which (II) and (III), colourless and yellow, respectively, were isolated in nearly equal proportion. The structure of the former anhydride was elucidated by decarboxylation of the derived dibasic acid to 6-methoxy-1-*m*-methoxyphenylnaphthalene (IV; R = Me, R′ = H),

* Part IV, preceding paper.

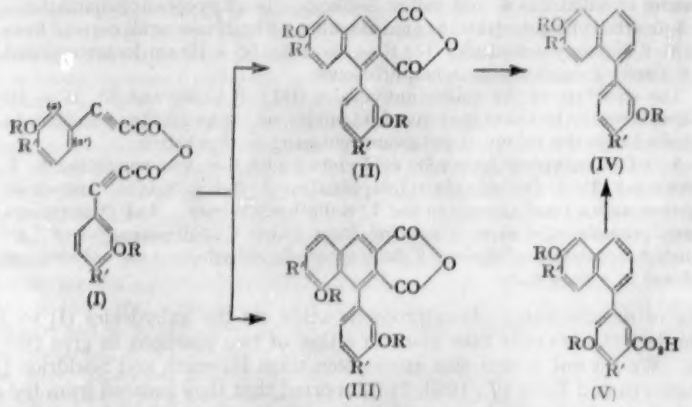
whose nitro-derivative was identical with one prepared by nitration of the product of decarboxylation of 3-methoxy-5-(6-methoxy-1-naphthyl)benzoic acid (V; R = Me, R′ = H).

m-Ethoxy- and *m-iso*propoxy-phenylpropiolic acid behaved analogously when similarly treated. The structure of the colourless anhydride (II; R = Et, R′ = H) was proved by decarboxylation of the derived dibasic acid to 6-ethoxy-1-*m*-ethoxyphenylnaphthalene (IV; R = Et, R′ = H), which was de-ethylated and then methylated to 6-methoxy-1-*m*-methoxyphenylnaphthalene. This gave a nitro-derivative identical with the authentic specimen. Attempted nitration of the product of decarboxylation of 6-ethoxy-1-*m*-ethoxyphenylnaphthalene-2 : 3-dicarboxylic or 3-ethoxy-5-(6-ethoxy-1-naphthyl)benzoic acid gave an inseparable mixture of nitro-derivatives.

The yellow anhydrides (III; R = Me or Et, R′ = H) cannot be *cyclo*butadiene derivatives (cf. Manthey, *Ber.*, 1900, **33**, 3081), for the solution of the derived acids in sodium hydrogen carbonate failed to discharge the colour of potassium permanganate solution (cf. Bucher, *J. Amer. Chem. Soc.*, 1908, **30**, 1244; Baddar, *J.*, 1947, 224; 1948, 1267). Moreover, they cannot be 2-phenylnaphthalene derivatives, since they were insoluble in boiling sodium carbonate solution and dissolved only in hot sodium hydroxide solution to give dibasic acids, which were converted back into the corresponding anhydrides on mere boiling with acetic anhydride. Furthermore, they gave imides when fused with solid ammonium carbonate (cf. Baddar, *loc. cit.*). The anhydrides must therefore be the isomers (III; R′ = H, R = Me and Et, respectively).

The structures of the two *iso*propoxy-anhydrides were assumed by analogy.

3 : 4-Diethoxyphenylpropiolic acid, when heated with acetic anhydride, gave yellow 6 : 7-diethoxy-1-(3′ : 4′-diethoxyphenyl)naphthalene-2 : 3-dicarboxylic anhydride (II; R = Et, R′ = OEt) together with a small amount of the colourless 7 : 8-diethoxy-isomer (III; R = Et, R′ = OEt). The isolation of (III; R = Et, R′ = OEt) threw some doubt on the results of Haworth and Sheldrick (*loc. cit.*) and Haworth and Kelly (*loc. cit.*). 3 : 4-Dimethoxyphenylpropiolic acid was therefore treated under the same conditions as those used by Haworth and Sheldrick (*loc. cit.*); the product had m. p. 305—309°, raised to 316—317° by repeated crystallisation from nitrobenzene or *o*-dichlorobenzene, so it was assumed to be a mixture of the two possible isomers, and the same would apply to



Haworth and Sheldrick's product (m. p. 305—306°). However, from 3 : 4-methylenedioxyphenylpropiolic acid both 6 : 7-methylenedioxy- and 7 : 8-methylenedioxy-1-(3′ : 4′-methylenedioxyphenyl)naphthalene-2 : 3-dicarboxylic anhydride were isolated. The latter, m. p. 280—282°, was obtained in very small amount (unpublished work by Baddar, Fahim, and Fleifel), and depressed the m. p. of the former; Haworth and Kelly (*loc. cit.*) reported the isolation of the former only.

m-Nitrophenylpropiolic acid gave under the same conditions a resinous, uncrystallisable material.

The structure of these anhydrides was supported by the fact that each coloured isomer of type (III) shows three maxima: R = Me, λ 342, 360, 378; R = Et, λ 343·5, 362, 381; and R = Pr^{i}, λ 346·5, 364, 384 mμ. The colourless isomers (II) possess inflexions at 320 mμ (unpublished work by Baddar and Sawires).

These results can be interpreted according to the annexed scheme (cf. Baddar and El-Assal, *J.*, 1951, 1844). The isolation of (II; R′ = H) and (III; R′ = H) in nearly equal proportions indicates that both carbon atoms (*a*) and (*a*′) are similarly activated, and that the group OR exerts an insignificant steric effect. However, the introduction of another alkoxyl group (R′) in position 4 enormously reduces the amount of the isomer (III; R = Et, R′ = OEt). Since that cannot be due to electronic factors, as both position (*a*) and (*a*′) are similarly affected by this group, it is most probably due to steric factors. The group R′ has apparently forced the group OR out of its position, and thus increased the steric influence of the OR group. As the methylenedioxy-group exhibits the same phenomenon, the effect of the group R′ on OR is more probably repulsive in origin (cf. Wheland, "Advanced Organic Chemistry," J. Wiley and Sons, New York, 1949, p. 207).

Experimental

m-iso*Propoxybenzaldehyde*.—A solution of *m*-hydroxybenzaldehyde (18·3 g.; 1 mol.) in 7·5% (w/w) alcoholic sodium ethoxide (60 ml.) was refluxed with *iso*propyl iodide (38·3 g.; 1·5 mol.) for 4 hr. The alcohol was evaporated, and the residue diluted with water and extracted with ether. The product was distilled to give *m-iso*propoxybenzaldehyde (61%), b. p. 121°/10 mm., 134°/28 mm. Morris (*J.*, 1950, 1915) gave b. p. 110—113°/2 mm. Its 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in red plates, m. p. 181—182° (Found: N, 15·9. $C_{16}H_{16}O_8N_4$ requires N, 16·3%).

Preparation of the Cinnamic Acids.—A mixture of the benzaldehyde (0·1 mole), malonic acid (0·15 mole), ethyl alcohol (20 ml.), and pyridine (2·5 ml.) was heated on a boiling-water bath for 7—8 hr. The mixture was cooled in ice, and the solid triturated with ethyl alcohol (*ca.* 10 ml.) and filtered off. It was washed with dilute hydrochloric acid, then crystallised from alcohol (cf. Walling and Wolfstirn, *J. Amer. Chem. Soc.*, 1947, **69**, 852). *m*-Methoxycinnamic acid had m. p. 117° (84%) (Jones and James, *J.*, 1935, 1600, recorded the same m. p.), *m*-ethoxycinnamic acid, m. p. 133° (93%) (Werner, *Ber.*, 1895, **28**, 2001, gave m. p. 122°), m-iso*propoxycinnamic acid*, m. p. 100—101° (98%) (Found: C, 69·6; H, 6·5. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%), and 3 : 4-diethoxycinnamic acid, m. p. 156° (70%) (Ide and Buck, *J. Amer. Chem. Soc.*, 1937, **59**, 726, gave the same m. p.). *m*-Nitrocinnamic acid, m. p. 196—197°, was obtained in 90% yield after 4 hours' heating (Tiemann and Oppermann, *Ber.*, 1880, **13**, 2060, gave the same m. p.).

αβ-*Dibromo*-m-*ethoxy-* *and* -m-iso*propoxy-cinnamic Acid*.—A carbon tetrachloride solution of bromine (1 mol.) was added dropwise to a boiling solution of the cinnamic acid (1 mol.) in dry carbon tetrachloride, exposed to direct sunlight. When bromination was complete (0·5—1 hr.), the precipitate was filtered off and the mother-liquor was evaporated at room temperature. αβ-*Dibromo*-m-*ethoxycinnamic acid* formed needles, m. p. 171—172° (73%) (from benzene) (Found: Br, 45·8. $C_{11}H_{12}O_3Br_2$ requires Br, 45·5%), and the m-iso*propoxy-acid* cubes, m. p. 130—131° (77%) [from toluene–light petroleum (b. p. 50—60°)] (Found: Br, 42·4. $C_{12}H_{14}O_3Br_2$ requires Br, 43·7%).

Methyl αβ-*Dibromo*-m-iso*propoxycinnamate*.—A stirred solution of methyl *m-iso*propoxycinnamate (15·5 g.; 1 mol.) (b. p. 166—168°/10 mm.) in carbon tetrachloride (50 ml.) was brominated in sunlight (4 ml. of bromine). The pale yellow oil left on evaporation of the solvent at room temperature was used for dehydrobromination without purification.

Methyl αβ-*Dibromo*-3 : 4-*diethoxycinnamate*.—An ice-cold, stirred solution of methyl 3 : 4-diethoxycinnamate [prepared from the acid chloride and methyl alcohol (cf. Kindler and Peschke, *Zentr.*, 1934, **105**, *I*, 2582)] in chloroform was brominated as usual. The chloroform was evaporated at room temperature; the residue crystallised from light petroleum (b. p. 100—120°) to give *methyl* αβ-*dibromo*-3 : 4-*diethoxycinnamate*, m. p. 110—111° (Found: Br, 39·5. $C_{14}H_{18}O_4Br_2$ requires Br, 39·0%) (yield, quantitative).

m-*Methoxy-*, m-*Ethoxy-*, *and* 3 : 4-*Dimethoxy-phenylpropiolic Acid*.—A mixture of the

corresponding dibromocinnamic acid (5 g.) and 25% methyl-alcoholic potash (20 ml.) was evaporated with stirring on a boiling-water bath to dryness. The residue was dissolved in water (charcoal), filtered, cooled, and acidified (cf. Reimer, *J. Amer. Chem. Soc.*, 1942, **64**, 2510). *m*-Methoxyphenylpropiolic acid had m. p. 109—110° (67%) [from chloroform–light petroleum (b. p. 50—60°)] (Jones and James, *loc. cit.*, gave m. p. 109°), and m-*ethoxyphenylpropiolic acid* m. p. 120° (74%) (Found: C, 69·0; H, 5·1. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3%). 3 : 4-Dimethoxyphenylpropiolic acid (yield, 50% from the ethyl ester) (crystallised from benzene–chloroform, the chloroform being evaporated off on the water-bath) had m. p. 150—151° (decomp.). Perkin and Schiess (*J.*, 1904, **85**, 165) gave m. p. 149°.

m-iso*Propoxy- and* 3 : 4-*Diethoxy-phenylpropiolic Acid.*—The corresponding methyl αβ-dibromocinnamate (0·1 mole) was refluxed with a solution of potassium hydroxide (0·7 mole) in absolute ethyl alcohol (200 ml.) for 7—8 hr. The diluted mixture was cooled in ice and acidified. The precipitate was extracted with ether, then re-extracted by sodium carbonate solution, and the alkaline solution cooled and acidified. The material extracted with chloroform was crystallised from light petroleum (b. p. 80—100°), forming pale cream needles (31%), m. p. 92—93°, of m-iso*propoxyphenylpropiolic acid* (Found: C, 70·3; H, 5·8. $C_{12}H_{12}O_3$ requires C, 70·6; H, 5·9%). 3 : 4-*Diethoxyphenylpropiolic acid* (50%) (from benzene) had m. p. 131° (decomp.) (Found: C, 67·0; H, 6·1. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%); this acid was also prepared from the dibromocinnamic ester in 45% yield by the rapid method described above.

m-*Nitrophenylpropiolic Acid.*—αβ-Dibromo-*m*-nitrocinnamic acid (35·5 g.) was left with 10% aqueous sodium hydroxide (80 ml.) at room temperature overnight. The precipitate obtained on acidification was treated with bromine in chloroform (Reich and Koehler, *Ber.*, 1913, **46**, 3727), and the α-bromo-acid (9 g.) was then converted into *m*-nitrophenylpropiolic acid (79%) by 10% aqueous sodium hydroxide (53 ml.) at room temperature overnight (*idem, ibid.*).

Self-condensation of m-*Methoxyphenylpropiolic Acid.*—The acid (5 g.) was refluxed with acetic anhydride (10 ml.) for 3 hr., and the cold solution then diluted with ether and left overnight. The yellow precipitate (3·5 g.; 74%) was washed with ether and the solution in glacial acetic acid (25 ml.) left overnight. The precipitate was repeatedly crystallised from glacial acetic acid, giving yellow 8-*methoxy*-1-m-*methoxyphenylnaphthalene*-2 : 3-*dicarboxylic anhydride* (*ca.* 1 g.), m. p. 230—230·5° (Found: C, 70·9; H, 4·0. $C_{20}H_{14}O_5$ requires C, 71·9; H, 4·2%). It was soluble in benzene and in boiling 20% sodium hydroxide solution but practically insoluble in ether. Its alkaline solution did not discharge the colour of potassium permanganate. The *dimethyl* ester had m. p. 123—125° [from light petroleum (b. p. 80—100°)] (Found: C, 69·2; H, 5·1. $C_{22}H_{20}O_6$ requires C, 69·5; H, 5·25%). Its *imide*, prepared by heating the anhydride (0·5 g.) with ammonium carbonate (10 g.) at 240—250° (cf. Baddar, *loc. cit.*), had m. p. 208·5—210° (Found: N, 4·55. $C_{20}H_{15}O_4N$ requires N, 4·2%).

A second crop, m. p. 165—185°, obtained from the acetic acid solution, crystallised from the same solvent to give colourless 6-*methoxy*-1-m-*methoxyphenylnaphthalene*-2 : 3-*dicarboxylic anhydride* (*ca.* 1 g.), m. p. 179—179·5° (Found: C, 71·7; H, 4·1%), moderately soluble in acetic acid, soluble in benzene, and insoluble in ether; it dissolved easily in cold 20% sodium hydroxide solution.

The mixed m. p. of the two isomers was 160—200° which was that of the original crude condensation product.

5-*Acetamido*-2-*naphthol.*—A mixture of 6-hydroxy-1-naphthylamine hydrochloride (19·5 g.) (from the base, prepared according to Brown *et al.*, *J. Amer. Chem. Soc.*, 1929, **51**, 1766), fused sodium acetate (10 g.), glacial acetic acid (20 ml.), and acetic anhydride (10 ml.) was warmed gently with stirring on the water-bath for 1 min. The acetyl derivative was precipitated with water and crystallised from alcohol, forming needles, m. p. 215—216° (cf. Sachs, *Ber.*, 1906, **39**, 3025).

1-*Acetamido*-6-*methoxynaphthalene.*—Methyl sulphate (50 g.) was slowly added to a stirred solution of 5-acetamido-2-naphthol (40 g.) in methyl alcohol (100 ml.), the solution being kept alkaline by dropwise addition of 9% sodium hydroxide solution. The stirred mixture was kept for a further hr., and diluted with water; the precipitated ether crystallised from alcohol (yield, 70%) and had m. p. 140° (cf. Sachs, *loc. cit.*).

6-*Methoxy*-1-*naphthylamine Hydrochloride.*—The above acetyl derivative (43 g.) was refluxed for 1 hr. with 25% methyl-alcoholic sodium hydroxide (100 ml.); the mixture was diluted with water, and the base hydrochloride precipitated from the dried ether extract with dry hydrogen chloride. The free base crystallised from light petroleum (cf. Cohen, Cook, Hewett, and Girard, *J.*, 1934, 653).

5-*Bromo*-3-*nitrobenzoic Acid.*—A mixture of *m*-nitrobenzoic acid (42 g.), concentrated

sulphuric acid (500 ml.), silver sulphate (39·2 g.), and bromine (15·5 ml.) was stirred at 100° for 7—8 hr. (cf. Derbyshire and Waters, *J.*, 1950, 573). The mixture was poured on ice, and the solid filtered off and extracted with sodium carbonate solution. 5-Bromo-3-nitrobenzoic acid was precipitated on acidification and formed needles (yield, 80%), m. p. 162°, from dilute alcohol. Hübner (*Annalen*, **1884**, **222**, 166) and Blanksma (*Chem. Weekblad*, **1912**, **9**, 862) gave m. p.s 161° and 162°, respectively.

3-Amino-5-bromobenzoic Acid.—Concentrated hydrochloric acid (65 ml.) was gradually added to 5-bromo-3-nitrobenzoic acid (37 g.) and tin (35·5 g.), and the mixture heated on a boiling-water bath for 2—3 hr. The product was made slightly alkaline with ammonia solution and filtered, and the filtrate treated with acetic acid till just acid. The precipitate gave colourless 3-amino-5-bromobenzoic acid, m. p. 220—222°, on crystallisation from alcohol. Hübner (*loc. cit.*), and McAlister and Kenner (*J.*, 1928, 1913), gave m. p.s 215° and 220—222°, respectively.

5-Bromo-3-hydroxybenzoic Acid.—The amino-acid (21·6 g.), in 10% (v/v) sulphuric acid (200 ml.), was diazotised with sodium nitrite (7 g.), and the solution boiled with dilute sulphuric acid (1 : 1, v/v) (120 ml.) for 15 min. The precipitated acid was crystallised from water, *5-bromo-3-hydroxybenzoic acid* being obtained in needles, m. p. 238—239° (yield nearly quantitative) (Found : C, 38·8; H, 2·55; Br, 36·8. $C_7H_5O_3Br$ requires C, 38·7; H, 2·3; Br, 36·9%).

5-Bromo-3-methoxybenzoic Acid.—This acid was prepared with methyl sulphate and after crystallisation from alcohol had m. p. 190—191° (73%) (Found : Br, 34·6. $C_8H_7O_3Br$ requires Br, 34·6%). Its methyl ester (from the acid chloride and methyl alcohol) had b. p. 156—157°/4 mm.

5-Methoxy-3-(6-methoxy-1-naphthyl)benzoic Acid.—1-Iodo-6-methoxynaphthalene (5·7 g.; 1 mol.) (cf. Cohen, Cook, Hewett, and Girard, *loc. cit.*) was heated with methyl 5-bromo-3-methoxybenzoate (4·9 g.; 1 mol.) and copper-bronze (7·5 g.) at 230—240° for 4 hr., and the product worked up as reported by Baddar and Gindy (*J.*, 1948, 1231). The benzene solution, after being freed from the diphenic acid, was evaporated, and the residue was esterified (diazomethane) and distilled. The fraction, b. p. 260—270°/4 mm. (0·62 g.), was hydrolysed with alcoholic potassium hydroxide, the solution acidified, and the precipitate dried in a vacuum at 100° for about 2 hr. On repeated crystallisation from methyl alcohol, the *benzoic acid* formed cubes (10%), m. p. 166—167° (shrinking at 162°) (Found : C, 73·5; H, 5·2%; *M*, 278. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%; *M*, 308). Inferior results were obtained if condensation was effected at 260—270°.

6-Methoxy-1-m-methoxyphenylnaphthalene.—(i) The benzoic acid (0·5 g.), quinoline (5 ml.), and copper-bronze (0·1 g.) were stirred and gradually heated to 200—210°. Copper-bronze (0·3 g.) was added portionwise during 1 hr. and the mixture heated for a further hr. The brownish-yellow 6-methoxy-1-*m*-methoxyphenylnaphthalene (0·24 g.) had b. p. 220—230°/4 mm. It was identified as the x-*mononitro*-derivative (cf. Baddar and El-Assal, *J.*, 1948, 1267), which crystallised from methyl alcohol in yellow crystals, m. p. 170—172° (Found : N, 4·9. $C_{18}H_{15}O_4N$ requires N, 4·53%).

(ii) 6-Methoxy-1-*m*-methoxyphenylnaphthalene-2 : 3-dicarboxylic acid (1·0 g.) was decarboxylated as in (i), to give 6-methoxy-1-*m*-methoxyphenylnaphthalene, b. p. 230—240°/4 mm. (0·23 g.). This gave a mononitro-derivative, m. p. and mixed m. p. with the above specimen, 170—172° (Found : N, 4·8%).

Condensation of m-*Ethoxyphenylpropiolic Acid.*—This acid (5 g.) was refluxed with acetic anhydride (12·5 ml.) for 3 hr., and treated as before. The precipitate was filtered off, and washed with ether (yield, *ca.* 4·0 g.; 83%); it had m. p. 135—160°. A hot benzene solution (*ca.* 25 ml.) slowly (45 min.) deposited colourless material which was separated by decantation; the m. p., 156—166°, was raised to 172—173° (*ca.* 1·3 g.) on repeated crystallisation from benzene. *6-Ethoxy-1-m-ethoxyphenylnaphthalene-2 : 3-dicarboxylic anhydride* (Found : C, 73·4; H, 4·6. $C_{22}H_{16}O_5$ requires C, 72·9; H, 5·0%) was soluble in hot acetic acid and in hot sodium hydroxide solution but practically insoluble in ether, and insoluble in sodium carbonate.

The original benzene mother-liquor was evaporated to dryness, and the residue was repeatedly crystallised from the minimum of acetic acid, giving *8-ethoxy-1-m-ethoxyphenylnaphthalene-2 : 3-dicarboxylic anhydride* (*ca.* 1·3 g.) in yellow crystals, m. p. 164—165°, depressed to 135—160° on admixture with the first isomer (Found : C, 72·5; H, 4·9%). It was insoluble in sodium carbonate, but soluble in boiling 20% sodium hydroxide solution to give a colourless disodium salt. The alkaline solution did not discharge the colour of potassium permanganate. Its *imide*, prepared as usual (at 210—220°) and crystallised from glacial acetic acid, was obtained in pale yellow crystals, m. p. 238·5—239·5° (Found : N, 4·5. $C_{22}H_{15}O_4N$ requires N, 3·9%).

1-Acetamido-6-ethoxynaphthalene.—5-Acetamido-2-naphthol (40 g.) was ethylated in 76%

yield with ethyl sulphate (61·6 g.) in a similar manner to that adopted for its methylation. On crystallisation from dilute alcohol, 1-*acetamido*-6-*ethoxynaphthalene* was obtained in needles, m. p. 155—156° (Found : C, 73·0; H, 6·4. $C_{14}H_{15}O_2N$ requires C, 73·4; H, 6·55%).

6-*Ethoxy*-1-*naphthylamine*.—An alcoholic solution (230 ml.) of the acetyl derivative (23·0 g.) was refluxed with concentrated sulphuric acid (46 ml.) for 1·5 hr., the mixture diluted with water, and the base liberated by sodium hydroxide. 6-*Ethoxy*-1-*naphthylamine* formed needles (53%) (from light petroleum), m. p. 104—105° (Found : N, 7·8. $C_{12}H_{13}ON$ requires N, 7·5%).

6-*Ethoxy*-1-*iodonaphthalene*.—This *compound*, prepared as usual (cf. Cohen, Cook, Hewett, and Girard, *loc. cit.*), formed a pale yellow oil, b. p. 182—184°/4 mm., 200—202°/10 mm. (30%), which solidified on cooling. It crystallised from light petroleum (b. p. 60—80°) in aggregates, m. p. 74—75° (Found : I, 41·8. $C_{12}H_{11}OI$ requires I, 42·6%).

3-*Bromo*-5-*ethoxybenzoic Acid*.—3-Bromo-5-hydroxybenzoic acid (21·7 g.) was ethylated in 70% yield with ethyl sulphate (31·0 g.) as usual; 3-*bromo*-5-*ethoxybenzoic acid* had m. p. 152° (from alcohol) (Found : Br, 33·0. $C_9H_9O_3Br$ requires Br, 32·7%). The *methyl ester* (from the acid chloride and methyl alcohol) formed needles (96%), m. p. 59—60° (from methyl alcohol) (Found : C, 46·8; H, 4·6. $C_{10}H_{11}O_3Br$ requires C, 46·3; H, 4·3%).

5-*Ethoxy*-3-(6-*ethoxy*-1-*naphthyl*)*benzoic Acid*.—This was prepared like the dimethoxy-compound (cf. Baddar and Gindy, *loc. cit.*). The intermediate ester was distilled and the fraction, b. p. 230—240°/4 mm. (0·55 g.), was hydrolysed with alcoholic potassium hydroxide. The acid precipitated on acidification was dried at 100° in a vacuum for 1 hr. and then crystallised from methyl alcohol to give the *ethoxybenzoic acid* (8%), m. p. 180—181° (Found : C, 74·9; H, 6·2. $C_{21}H_{20}O_4$ requires C, 75·0; H, 6·0%). The material insoluble in benzene was purified by repeated crystallisation from glacial acetic acid to give 3 : 3′-*diethoxydiphenyl*-5 : 5′-*dicarboxylic acid*, m. p. 293—294° (Found : C, 64·7; H, 5·4. $C_{18}H_{18}O_6$ requires C, 65·5; H, 5·45%).

Decarboxylation of 6-*Ethoxy*-1-m-*ethoxyphenylnaphthalene*-2 : 3-*dicarboxylic Acid*.—The acid was decarboxylated as described for the dimethoxy-dicarboxylic acid, and the product distilled, giving the pale yellow 6-ethoxy-1-*m*-ethoxyphenylnaphthalene, b. p. 210—220°/4 mm. This failed to solidify, and on nitration gave a mixture. Its structure was elucidated by heating it (0·25 g.) with magnesium iodide (from 0·2 g. of magnesium powder) at 210—220° for 2 hr. The dihydroxy-compound was then methylated with diazomethane, and the product was nitrated with nitric acid (*d* 1·42) in glacial acetic acid. The nitro-derivative was identical (m. p. and mixed m. p.) with the mononitro-derivative of 6-methoxy-1-*m*-methoxyphenylnaphthalene.

Condensation of m-iso*Propoxyphenylpropiolic Acid*.—The propiolic acid (2·7 g.) was refluxed with acetic anhydride (7 ml.) for 3 hr. The solution was concentrated under reduced pressure, and diluted with ether. The pale yellow precipitate was washed with ether and dried; it had m. p. 135—142° (1·7 g.; 63%). The mixture was dissolved in acetic acid (*ca.* 10 ml.) and left overnight. The precipitate consisted of two types of crystals which were mechanically separated : (*a*) fine yellow needles, m. p. 167—168°, and (*b*) slightly coloured aggregates, m. p. 156—158°. The mother-liquor was evaporated, and the residue crystallised from the minimum of acetic acid. One isomer (0·52 g.) was recrystallised from glacial acetic acid, giving 8-iso*propoxy*-1-m-iso*propoxyphenylnaphthalene*-2 : 3-*dicarboxylic anhydride* in fine yellow crystals, m. p. 172—173° (Found : C, 72·9; H, 5·6. $C_{24}H_{22}O_5$ requires C, 73·8; H, 5·6%). The 3′ : 6-*diiso*propoxy-isomer (0·52 g.) crystallised from glacial acetic acid in nearly colourless crystals, m. p. 163—164°, depressed to 135—142° on admixture with the first isomer (Found : C, 74·0; H, 5·5%). Neither isomer in alkaline solution discharged the colour of potassium permanganate. The constitution of the two isomers rested entirely on analogy.

Condensation of 3 : 4-*Diethoxyphenylpropiolic Acid*.—The propiolic acid (5 g.) was heated with acetic anhydride (12·5 ml.) on a boiling-water bath for 4 hr. and worked up as usual. The 6 : 7-*diethoxy*-1-(3′ : 4′-*diethoxyphenyl*)*naphthalene*-2 : 3-*dicarboxylic anhydride* (3·5 g.) crystallised from acetic acid in greenish-yellow crystals, m. p. 216—217° (Found : C, 69·0; H, 5·9. $C_{26}H_{26}O_7$ requires C, 69·3; H, 5·8%). The acetic anhydride–ether mother-liquor was concentrated, then decomposed with water. The precipitate was filtered off and extracted with dilute cold sodium carbonate solution. The residue, m. p. 154—184° (0·55 g.), was crystallised from acetic acid, and the product (0·4 g.), m. p. 200—214°, was repeatedly crystallised from acetic acid to give the 3′ : 4′ : 7 : 8-*tetraethoxy-anhydride* in colourless crystals, m. p. 220·5—222·5°, depressed to 194—195° on admixture with the first isomer (Found : C, 68·3; H, 5·9%). It was soluble in boiling 20% sodium hydroxide solution, and its alkaline solution did not discharge the colour of potassium permanganate.

Dimethyl 6 : 7-*Diethoxy*-1-(3′ : 4′-*diethoxyphenyl*)*naphthalene*-2 : 3-*dicarboxylate*, prepared by

use of diazomethane, crystallised from light petroleum (b. p. 80—100°) in colourless crystals, m. p. 130—131° (Found: C, 67·4; H, 6·12. $C_{28}H_{32}O_8$ requires C, 67·7; H, 6·45%).

Condensation of 3 : 4-*Dimethoxyphenylpropiolic Acid.*—The propiolic acid was heated with acetic anhydride as mentioned by Haworth and Sheldrick (*loc. cit.*). The precipitate (3·5 g.; from 5 g.), m. p. 305—309° (shrinking at 302°), was repeatedly crystallised from nitrobenzene or *o*-dichlorobenzene, giving 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)naphthalene-2 : 3-dicarboxylic anhydride in greenish-yellow crystals, m. p. 316—317° (shrinking at 314°) (Found: 66·8; H, 4·6. Calc. for $C_{22}H_{18}O_7$: C, 67·0; H; 4·6%). Haworth and Sheldrick (*loc. cit.*) gave m. p. 305—306°. The crystals showed extinction and pleochroism, probably belonging to the orthorhombic system.

The acetic anhydride–ether mother-liquor contained only unchanged 3 : 4-dimethoxyphenylpropiolic acid.

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Intermolecular Complex Formation between Iodine or Iodine Cyanide and Organic Molecules: Vibrational Spectra.

By D. L. GLUSKER and H. W. THOMPSON.

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The interaction between iodine or iodine cyanide on the one hand and a variety of organic molecules on the other, has been examined by measuring the infra-red vibrational spectra. The effect of dissolved iodine on the spectra of hydrocarbons, ketones, ethers, esters, ring ethers, pyridine, and picolines was first measured. Further details were usually obtained by dissolving both components in "inert" solvents (carbon disulphide and carbon tetrachloride). The results suggest that complex formation with the ketones and ethers occurs through the carbonyl group or ether-oxygen atoms. With pyridine and the picolines there is a more profound change which suggests a cleavage of the iodine molecule and formation of ions. Experiments with iodine cyanide gave similar results. By contrast with iodine, which has no infra-red absorption, iodine cyanide has three absorption bands, and the effect of complex formation upon these gives additional information. Preliminary studies have been made on the equilibrium constant for the iodine–dioxan complex formation and its variation with temperature.

THE differences in colour between solutions of iodine in different organic solvents have not yet been conclusively explained. That they arise from variations in the degree of molecular association of iodine as the solvent is changed is improbable, for although definite indications of association have been found, the same variation of apparent molecular weight with concentration occurs with such solvents as *cyclo*hexane and dioxan in which the difference of colour of iodine is marked (Kortüm and Friedheim, *Z. Naturforsch.*, 1947, **22**, 20). The suggestion that colloidal phenomena are responsible is also not substantiated by experimental results.

Of the two remaining theories, the first supposes that a cage of solvent molecules around the iodine molecule exerts a perturbing effect on its electronic energy levels, leading to spectral changes as the solvent is altered (Bayliss and Rees, *J. Chem. Phys.*, 1940, **8**, 377; Bayliss, *ibid.*, 1950, **18**, 292). The other assumes the formation of some type of intermolecular complex between solute and solvent (Benesi and Hildebrand, *J. Amer. Chem. Soc.*, 1949, **71**, 2703; Mulliken, *ibid.*, 1950, **72**, 600; 1952, **74**, 811; *J. Phys. Chem.*, 1952, **56**, 801). While it seems to us unjustifiable at present to regard the cage theory as having no experimental support, most of the results can be explained more satisfactorily by the second hypothesis.

In some cases, for example with pyridine or dioxan and iodine, crystalline compounds have been isolated (Rheinboldt and Boy, *J. pr. Chem.*, 1931, **129**, 273; Chatelet, *Compt.*

rend., 1933, **196**, 1421, 1907); Fairbrother (*J.*, 1936, **847**; 1948, 1051) first found direct evidence for the polarisation of iodine in non-polar solvents from measurements of dipole moment, and other workers have studied the electrical conductivity of such solutions (Audrieth and Birr, *J. Amer. Chem. Soc.*, 1933, **55**, 668; Kortüm and Wilski, *Z. physikal. Chem.*, 1953, **202**, 235). Hartley and Skinner (*Trans. Faraday Soc.*, 1950, **46**, 621) also found a marked parallelism between the heats of solution of iodine in organic solvents and the colour of the solutions. The visible and ultra-violet absorption spectra have also been measured, and are in accordance with the idea of complex formation (Benesi and Hildebrand, *J. Amer. Chem. Soc.*, 1948, **70**, 2832; 1949, **71**, 2703; 1950, **72**, 2273). Mulliken (*loc. cit.*) has surveyed the experimental results and has tried to systematise the various phenomena in terms of a theory of " outer " and " inner " complex formation, and the occurrence of " charge-transfer " complexes. In this formulation iodine is an " acceptor " and the organic molecule is a " donor."

It seemed likely that the infra-red absorption spectra might provide direct evidence for the nature of the intermolecular interaction, since the vibrational frequencies of the solvent will be affected, and the absence of vibrational absorption by iodine makes the circumstances favourable for this study. Mulliken has suggested, on quantum-mechanical grounds, the mode of interaction to be expected between iodine and certain solvent molecules, and this can be examined by observing which molecular vibration frequencies are most affected and which nuclei are therefore involved in the interaction.

Experiments were begun in this laboratory several years ago by Wood (Diss., Oxford, 1950) and have now been repeated in greater detail and extended to include iodine cyanide as solute. In the latter case, there is a particular additional advantage in that we can also examine the effect of any complex formation on the vibration frequencies of the solute, and as shown below this provides important information. A preliminary account of our work was published earlier (Glusker, Thompson, and Mulliken, *J. Chem. Phys.*, 1953, **21**, 1407) and similar measurements with hydrocarbons and with pyridine have been described by other workers (Pimentel, Jura, and Grotz, *ibid.*, 1951, **19**, 513; Ham, Rees, and Walsh, *Nature*, 1952, **169**, 110; *J. Chem. Phys.*, 1952, **20**, 1336).

Experimental

Iodine was resublimed and stored before use in a desiccator over phosphoric oxide. Iodine cyanide was prepared by adding iodine slowly to concentrated aqueous potassium cyanide, and the mixture kept for some hours in a refrigerator. The precipitate was filtered off, washed with ice-water, recrystallised from water, and resublimed.

Considerable care was taken to eliminate traces of water from the organic compounds and solvents used. The following substances were dried with anhydrous calcium sulphate and refractionated in an all-glass apparatus closed by a drying tube containing phosphoric oxide: acetone (b. p. 56·4—56·5°), *n*-hexyl methyl ketone (b. p. 173·5—174°), acetophenone (b. p. 200·0—200·2°), diethyl ketone (b. p. 101·1—101·3°), ethyl acetate (b. p. 76·8—77·0°). *cyclo*-Hexanone was separated from traces of *cyclo*hexanol by formation of its bisulphite addition compound, the latter being decomposed by aqueous sodium carbonate and the *cyclo*hexanone refractionated (b. p. 153·8—154°) and stored over anhydrous calcium sulphate. The following compounds were recrystallised from light petroleum–alcohol and dried in a vacuum-desiccator: benzophenone (m. p. 48—49°), benzil (m. p. 94·5—95·0°), dimethyl-4-pyrone (m. p. 132·5—133°), dibenzylideneacetone (m. p. 107—108°). " AnalaR " ether was redistilled (b. p. 34·4—34·6°) and stored over sodium. " AnalaR " dioxan was dried (KOH), refluxed over sodium, and finally distilled (b. p. 101·1—101·3°). Mesitylene was refluxed with sodium for 24 hr., fractionated (b. p. 166·6—167°), and stored over anhydrous calcium sulphate. " AnalaR " pyridine was dried for a week over potassium hydroxide, and distilled from and stored over barium oxide (b. p. 114·8—115°). Samples of α-, β-, and γ-picoline of high purity were obtained from the Chemical Research Laboratory, Teddington.

Carbon disulphide, acetonitrile, and carbon tetrachloride were purified in the standard way (Weissberger and Proskauer, " Organic Solvents," Oxford, 1935).

All the measurements were made with a Perkin–Elmer 12C spectrometer, prisms of lithium fluoride, rock-salt, and KRS 5 (thallium bromoiodide) being used. For most of the work the

absorption cell was made from a pair of rock-salt plates separated by an amalgam washer about 0·1 mm. thick. The filling holes could be sealed by Polythene plugs. For measurements at the very long wave-lengths, a cell made from thin Polythene sheets was used.

The formation of complexes was studied in two ways. First, the effect of the solute upon the pure solvent was measured, and secondly, the two components were mixed in an " inert " solvent. It was often possible to observe changes in the latter case which were obscured in the former by the intense absorption of one component, and it was also possible by using an " inert " solvent to study more satisfactorily changes of equilibrium as the concentrations and temperature were varied.

Special care was taken throughout to exclude atmospheric water vapour by preparing the solutions in a dry box, and as a test of this procedure some solutions were subsequently allowed to absorb moisture and the spectral effects examined.

Many of the observed spectral shifts were small, and it was therefore necessary to be certain of their reality. In general, the spectrum of a dilute solution of one component (*e.g.*, acetone) in carbon disulphide or carbon tetrachloride was recorded. The solution was then saturated with the second component (iodine or iodine cyanide) and its spectrum was superposed upon the former record. All measurements were made a few minutes after preparation of the solutions, and repeated some hours later.

A water-jacketed cell holder was also built, by means of which the spectra could be measured at temperatures between 15° and 50°, and attempts were made to study the change in equilibrium constants with temperature.

Results and Discussion

The vibrational spectra of saturated solutions of iodine in carbon disulphide or carbon tetrachloride are indistinguishable from those of the pure liquids. Also, the electronic spectra of these solutions are almost identical with that of iodine vapour (Benesi and Hildebrand, *loc. cit.*). These two solvents have therefore been assumed to behave as " inert " media and have been used as such for studying the complex formation between iodine or iodine cyanide and the " active " solvents.

The measurements reported by different workers for mesitylene–iodine are confusing. Pimentel, Jura, and Grotz (*loc. cit.*) first suggested that a number of new bands appear upon addition of iodine to mesitylene, but Ham, Rees, and Walsh (*loc. cit.*) could find no changes at all. Wood's measurements in this laboratory indicated that one new band appeared in the spectrum of mesitylene, near 1300 cm.$^{-1}$, and this has been confirmed by our later work which also revealed a noticeable change in intensity of a band near 880 cm.$^{-1}$. We have since been informed by Prof. Pimentel that his earlier results were unreliable because of impurities in the mesitylene used, and the failure of Ham, Rees, and Walsh to observe the band near 1300 cm.$^{-1}$ may have been due to its being very weak. The most plausible interpretation of our results with mesitylene is that the mutual interaction of the two molecules causes a breakdown of certain selection rules, enabling the vibration frequency near 1300 cm.$^{-1}$, which is active in the Raman effect, to appear in infra-red absorption. The alteration in the intensities of other bands such as that near 880 cm.$^{-1}$ could be explained similarly.

No spectral changes have been found on addition of iodine to benzene, toluene, xylenes, or dimethylnaphthalenes (Wood, *loc. cit.*). Similarly, no changes could be found in the spectrum of acetonitrile after addition of iodine, nor when the two components were mixed in an " inert " solvent. In view of the brown colour of the solution of iodine in acetonitrile, this result was surprising, and in the light of the other results given below a complex might have been expected, formed through the ·C⋮N group. It would appear that, if this occurs, the effect is not large enough to be noticed because of the high force constant of the ·C⋮N bond.

The effects found with many compounds containing the carbonyl group are more informative. Displacements of the stretching vibration band of this group were noticed when iodine was added to pure liquid ketones, but from measurements in an " inert " solvent the changes can be seen more clearly. Typical results were given in our earlier note (*J. Chem. Phys.*, 1953, **21**, 1407). In general a new band due to the complex appears,

lying about 20 cm.$^{-1}$ below that of the ketone itself. The relative intensity of the two bands changes as the concentrations of the two components are altered, as seen from the results in different " inert " media in which the solubilities are different. Apart from this effect in the carbonyl group band, the only spectral change found was the appearance in some cases of a weak band between 1200 and 1300 cm.$^{-1}$. It must therefore be concluded that the complex formation occurs essentially through the carbonyl link.

Now, since the only significant change in the spectra of these ketones after addition of iodine appears to involve the carbonyl group, it is unlikely that the change can be due to any chemical interaction which will lead to a new chemical species and to larger spectral changes. However, some measurements were carried out to discover whether the spectra of the solutions of iodine in the ketones changed over a long period. It was found that with ketones which have a methylene group adjacent to the carbonyl group, a slow irreversible reaction can occur, which is moreover accelerated by the presence of small amounts of water. With acetone, the new spectrum showed many similarities to that of iodoacetone, for which the frequency of the carbonyl group stretching vibration lies somewhat higher (*ca.* 1725 cm.$^{-1}$) than that of acetone itself. This rise in frequency is to be contrasted with the fall previously noticed in the initial complex formation. There is a similar slow reaction with dibenzylideneacetone, and with *cyclo*hexanone the chemical process proceeds too rapidly for the characteristics of the initial complex to be seen.

With benzophenone, where there are no reactive methylene groups, the spectrum of the mixture with iodine remains constant with time, and shows the pair of bands due to the carbonyl groups of the free molecule and the complex. With benzil, a new band near 1656 cm.$^{-1}$ appears after addition of iodine, but its intensity relative to the normal carbonyl group band near 1678 cm.$^{-1}$ is much lower than in the case of benzophenone. This point is discussed below.

Complex formation was also studied by using molecules containing an ether-type oxygen atom. Ham, Rees, and Walsh found no spectral changes with ethers, but using dilute solutions of ether in " inert " solvents saturated with iodine, we have found a new band near 1098 cm.$^{-1}$ linked with that of ether itself at 1119 cm.$^{-1}$. Exactly the same pair of bands at 1098, 1119 cm.$^{-1}$ are found for the dioxan–iodine system, where there is another new band at 830 cm.$^{-1}$ linked with the ring-ether band at 874 cm.$^{-1}$. Addition of iodine to tetrahydrofuran also produces new bands near 1052 and 842 cm.$^{-1}$. In all these cases the spectra of the mixed solutions remain constant with time.

TABLE 1.

Acceptor = iodine. Donor = Dimethyl-4-pyrone.
N = new band (cm.$^{-1}$). I = change of band intensity.

15% Donor in CS_2 sat. with I_2		15% Donor in CCl_4 sat. with I_2		Probably associated with band at	15% Donor in CS_2 sat. with I_2		15% Donor in CCl_4 sat. with I_2		Probably associated with band at
N	I	N	I		N	I	N	I	
—	2957	—	—	—	1329	—	1329	—	1325
—	2922	—	—	—	—	1193	—	1193	—
—	2850	—	—	—	1161	—	1161	—	1155
—	2800	—	—	—	1032	—	1032	—	1029
—	2782	—	—	—	—	952	—	953	—
1658	—	1658	—	1674	940	930	939	930	930
1580	—	1584	1635	1635?	897	—	898	—	891
1400	—	1401	—	1390	—	867	—	867	—
—	1367	—	1370	—	845	—	—	—	867?

With ethyl acetate, the carbonyl group frequency appears to be affected by iodine in the same way as with the ketones, but the bands connected with the ether-type part of the molecule (·C·O·C_2H_5) are not influenced like those in the ethers themselves. With dimethyl-4-pyrone, on the other hand, changes occur across the entire spectrum (Table 1, Fig. 1), suggesting that interactions may occur through both the carbonyl group and the ring-ether oxygen atom. The spectrum of the mixture is constant with time.

The specific spectral shifts found above with all the ketones and ethers point to a mechanism of complex formation by electron donor and acceptor between the organic

molecule and iodine. This would correspond to the formation of an " outer complex " in the sense discussed by Mulliken. He further suggested that in these structures formed from an iodine molecule and a carbonyl group, the iodine atoms should lie in the plane of the group (I), with their internuclear axis perpendicular to the C=O bond. Benzil has two adjacent carbonyl groups and a structure which will hinder the approach of an iodine molecule if the orientation just mentioned has to be achieved, whereas if the axis of the iodine molecule were to lie perpendicular to the plane of the group (I) no such hindrance would arise. It is therefore worth noting that with benzil the intensity of the new band due to the complex is abnormally low, and this may indicate greater difficulty of its formation.

(I)

TABLE 2.

Acceptor = iodine. N = New band. I = Intensity change.
d = donor. Band positions in cm.$^{-1}$.

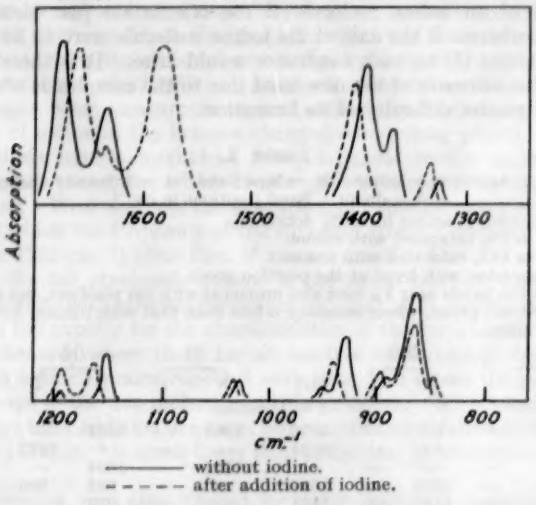
(i) Saturated solution of iodine in 100% donor.
(ii) 15% Donor in CS_2 saturated with iodine.
(iii) 15% Donor in CCl_4 saturated with iodine.
(iv) Probably associated with band at the position given.
(Some changes in the bands near 3 μ were also measured with the picolines, but since these were only examined with a rock-salt prism, where accuracy is less than that with lithium fluoride, the results are not included in the table.)

(i)		(ii)		(iii)			(i)		(ii)		(iii)		
N	I	N	I	N	I	(iv)	N	I	N	I	N	I	(iv)
						d = Pyridine.							
3065	3076	—	—	—	—	3076	1060	—	1064	—	—	—	1067
3028	—	—	—	—	—	3024	—	—	—	1027	—	—	—
—	2998	—	—	—	—	—	1005	—	1004	—	—	—	—
—	—	—	—	1628	—	1616	—	—	993	990	—	—	990
1453	—	—	—	1446	—	1441	—	—	973	—	—	—	—
—	1351	—	1350	—	1350	—	—	—	938	—	—	—	—
1241	1239	—	—	—	—	—	*ca.* 755	—	745	—	—	—	742
1207	—	1208	—	—	—	1215	—	—	705—	—	—	—	711—
—	—	1150	—	—	—	1144			692				692
						d = α-Picoline.							
—	—	—	—	—	1452	—	—	—	—	1035	—	—	—
—	—	—	—	1423	1432	1432	—	1021	—	—	—	—	—
—	—	1379	—	1378	—	1375	1010	—	1008	—	—	—	—
—	1237	1237	—	—	—	1232	986	—	983	—	—	—	999
—	—	1207	—	—	—	1232	801	—	801	—	—	—	798
—	—	1150—	—	—	—	1146	—	—	757—	—	—	—	753—
		1155							743				740
1109	—	1107	1100	—	—	1100	714	—	714	—	—	—	724
—	—	1054	—	—	—	1045							
						d = β-Picoline.							
2490	2450	2490	—	—	—	2450	1099	—	1098	1103	—	—	1103
1591	—	—	—	—	—	1572	1050	—	1049—	—	—	—	1041
—	—	1258	1240	—	—	1225?			1058				
—	1228	—	1225	—	—	—	—	—	—	1028	—	—	—
1187	—	1187	1190	—	—	1190	—	—	913	—	—	—	923
—	1168	1161	—	—	—	1168	816	—	786—	—	—	—	780
1122	1126	—	1125	—	—	1125			803—814				
							700	—	694	705	—	—	705
						d = γ-Picoline.							
2480	—	2380—	—	—	—	2440	1011	—	1008	993	—	—	993
		2470					—	—	968	—	—	—	965
—	—	1608	1598	1608	1598	1598	870	872	—	—	—	—	872
1243	1210—	1240	1210—	—	—	1210—	—	—	805	793—	—	—	793—
	1218		1218			1218				799			799
—	1168	—	—	—	—	—	709	—	705—	715—	—	—	715—
1064	1069	1067	1069	—	—	1069			710	719			719
1025	—	—	1037	—	—	1037?							

The spectra of solutions of iodine in pyridine and the picolines show very marked changes from those of the pure solvents. The positions of the bands for pyridine, α-picoline, and β-picoline are given in Table 2, and the manifold changes of intensity are shown in Fig. 2.

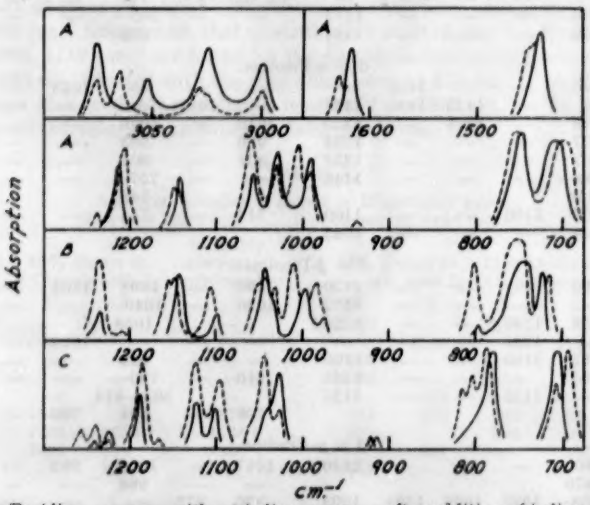
The spectra of the mixtures were unchanged after long storage, and although elaborate precautions were taken here to exclude traces of water, it was found that the addition of a little water to a pyridine–iodine solution did not affect the results.

FIG. 1. *Dimethyl-γ-pyrone and iodine in carbon disulphide or carbon tetrachloride.*



——— without iodine.
– – – – – after addition of iodine.

FIG. 2. *Pyridine and picolines with iodine in carbon disulphide or carbon tetrachloride.*



A. Pyridine ——— without iodine, – – – – – after addition of iodine.
B. α-Picoline ——— without iodine, – – – – – after addition of iodine.
C. β-Picoline ——— without iodine, – – – – – after addition of iodine.

With γ-picoline, addition of iodine caused a similar set of changes, listed in Table 2, but a rapid reaction soon set in and the whole mixture solidified. Efforts were made to establish the products of this reaction by solvent extraction, by analysis, and from spectra, but no definite conclusions were reached. There are, however, indications that salts of

the type $[\gamma\text{-Pic—I}]^+ I^-$ are present, complicated by ionic solvation with the picoline molecule.

The spectral changes involved in the addition of iodine to pyridine and its homologues are so strikingly greater than those found previously with the ketones and ethers as to suggest some essentially different feature in the formation of the complexes. Whereas with the ketones the only significant change of frequency appears to concern the carbonyl group, many vibrations of the pyridine ring seem to be affected. This may imply that an essentially new structure of markedly different electronic configuration, such as the $[Py–I]^+$ ion, has been produced. In the lists of heats of solution quoted by Hartley and Skinner (*loc. cit.*), pyridine occupied an extreme place. Also, measurements using radioactive iodine have suggested that exchange with iodine in a pyridine–iodine complex is complete immediately after mixing (Kleinberg and Sattizahn, *J. Amer. Chem. Soc.*, 1951, **73**, 1865).

In order to examine this further, the spectrum of the pyridine–iodine complex in carbon disulphide was measured over a wide range of concentrations of the two components. The concentration of pyridine was varied between 0·005 and 3·0M, and that of iodine between 0·0005 and 0·5M. If there is a transition point between the " outer " and " inner " complex, as suggested by Mulliken, it might be observed in this way. The visible absorption band of iodine in pyridine–heptane solutions shifts appreciably as the concentration of pyridine changes from 0·01 to 10·0M, and there are signs that the onset of the shift occurs at about 0·1M (Reid and Mulliken, personal communication). If this is true, and if the shift is linked with the transition from " outer " to " inner " complex, we might expect to find corresponding changes in the vibrational spectrum. In fact, our results failed to reveal any spectral alterations which could be interpreted in this way.

Having regard to the results of Fairbrother (*loc. cit.*) which showed that there is a polarisation of iodine in many non-polar solvents and even in some hydrocarbons, we might regard the formation of a charge-transfer complex as applicable to all the above cases, with pyridine and picolines in an extreme class in which ionisation is complete. Further information was sought by using iodine cyanide as the " acceptor " molecule, for we can follow here not only the vibrational spectrum of the " donor," but also that of the " acceptor," and complete cleavage of the iodine cyanide molecule into ions should be directly observable.

The infra-red spectrum of iodine cyanide dissolved in carbon tetrachloride or carbon disulphide gives as fundamental vibration frequencies $\nu_1 = 462$ cm.$^{-1}$, $\nu_3 = 2167$ cm.$^{-1}$, $\nu_2 = 315$ cm.$^{-1}$, corresponding to the values 470, 2158, and 321 cm.$^{-1}$ obtained from the Raman spectrum in methanol (West and Farnsworth, *J. Chem. Phys.*, 1933, **1**, 402). Addition of benzophenone to a saturated solution of iodine cyanide in carbon tetrachloride causes the band at 2167 cm.$^{-1}$ (ν_3), largely controlled by the C≡N link, to shift to 2162 cm.$^{-1}$, and when benzophenone is added to a saturated solution of iodine cyanide in carbon disulphide the band at 462 cm.$^{-1}$ (ν_1), largely controlled by the C–I link, shifts to 458 cm.$^{-1}$. It was impossible to study the effect on the bending vibration ν_2 because of overlapping absorption by benzophenone.

Similarly in carbon disulphide, the addition of dioxan to iodine cyanide shifts the band at 462 cm.$^{-1}$ to 456 cm.$^{-1}$, and that at 315 cm.$^{-1}$ to 326 cm.$^{-1}$.

All these small shifts indicate the formation of a weak complex which affects the vibration of the whole iodine cyanide molecule.

When pyridine is added to a solution of iodine cyanide in carbon disulphide or carbon tetrachloride, all the bands of iodine cyanide diminish in intensity as the addition proceeds, and finally disappear. There are no signs of fresh bands displaced from those of iodine cyanide, although it is just possible that if these were weak they might be masked by bands of pyridine. This behaviour is in contrast to that observed with a ketone or ether as " donor " molecule, and strengthens the previous hypothesis that in the case of pyridine complexes a definite split has occurred, probably leading to $[Py–I]^+$ and $[CN]^-$ ions. We might expect to detect a vibration band of the $[CN]^-$ ion, but none has been found, probably because of intense absorption by the other species present. The formation of $[Py–I]^+$ rather than $[Py–CN]^+$ ions is supported by Fairbrother's results on the

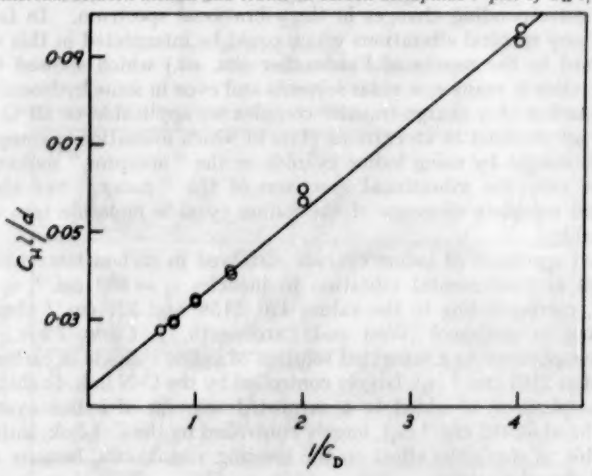
TABLE 3.

Acceptor = iodine cyanide. d = Donor.
N = new band (cm.$^{-1}$), I = change of band intensity.

15% d in CS_2 sat. with ICN		Probably connected with band at (cm.$^{-1}$)	15% d in CS_2 sat. with ICN		Probably connected with band at (cm.$^{-1}$)
N	I		N	I	
	d = Pyridine.			d = Dimethyl-4-pyrone.	
1235	—	1215	1662	—	1674
1210	—	1215	1590	1631	1631
1150	—	1144	1400	—	1390
1065	—	1067	1372	—	1366
1030	—	1027	1329	—	1325
1002	990	990	—	1193	1193
940	—	—	1161	—	1155
747	—	742	1032	—	1029
705—692	—	711—692	956	—	953
			939	—	930
			898	—	891
			863	—	862

polarisation of iodine cyanide in pyridine, and also by the fact that the changes in the spectrum of pyridine caused by addition of iodine cyanide (Table 3) are almost identical with those which occur when iodine is added.

FIG. 3. *Equilibrium between dioxan and iodine in carbon disulphide: plot of* $C_{\mathrm{II}}\,l/d$ *against* $1/C_{\mathrm{D}}$.



The addition of iodine cyanide to dioxan, benzophenone, or dimethyl-4-pyrone leads to spectral changes exactly similar to those already found with iodine.

Preliminary measurements have been made of the equilibrium constants for the complex formation between iodine or iodine cyanide on the one hand and ketonic or ether compounds on the other. Qualitatively, the band intensities show that the complexes are more easily formed with iodine cyanide than with iodine. The case of iodine–dioxan has been studied by means of the band at 830 cm.$^{-1}$ associated with the complex, which is assumed to be 1 : 1 in composition. Then at 830 cm.$^{-1}$,

$$d = \text{optical density} = \varepsilon \,.\, C_x \,.\, l$$

in which ε is the extinction coefficient, l the path length, C_x the concentration of complex, and d is the optical density. The equilibrium constant $K = C_x/C_1C_2$, in which C_1, C_2 are the concentrations of free dioxan and free iodine, respectively. If C_{D}, the total con-

centration of dioxan, is much greater than C_H, the concentration of iodine, then $C_1 = C_D$ and $C_2 = (C_H - C_x)$ and it follows that

$$C_H l/d = 1/KεC_D + 1/ε$$

In Fig. 3 the left-hand side of this equation is plotted against $1/C_D$, and from the slope and intercept we obtain $K \sim 0{\cdot}7$ at 25°. From a series of such determinations at different temperatures, it was possible to calculate a value for the heat of formation of the complex, the result being roughly 5 kcal./mole. These results must be regarded as uncertain owing to errors in determining the intensity of the weak band of the complex. More accurate measurements are now being carried out with a double-beam spectrometer, and particularly on complexes with the carbonyl group near 5·8 μ.

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THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, June 1st, 1954.*]

Intensities of Vibration Bands. Part VI. Alkyl Esters.*

By R. A. RUSSELL and H. W. THOMPSON.

[Reprint Order No. 5519.]

The intensities of the vibrational absorption bands of some esters near 1200 cm.$^{-1}$ have been determined, extending previous results of Francis. Most of the compounds give approximately the same value for this intensity, although methyl esters show a small but significant difference. The composite nature of the band has been discussed and possible explanations have been suggested. The effect of different solvents upon the band intensity has been determined, and the values have been compared with that found in the gas phase. The results suggest that the Onsager relation for the intensity in the two phases is satisfactory.

THE use of molecular vibration frequencies in structural diagnosis is well established. Interest is now moving towards the use of vibrational band intensities to provide further structural information, but the best way of doing this cannot be assessed until more is known about the strength of key absorption bands in different molecules or of a given band in different physical environments. The intensities of several absorption bands of esters and ketones were recently determined by Francis (*J. Chem. Phys.*, 1951, **19**, 942). While his main interest lay in the band due to CH_3 and CH_2 groups, Francis also gave values for the bands near 1720 and 1200 cm.$^{-1}$ in a few molecules. The former band is characteristic of the stretching vibration of the carbonyl groups. That near 1200 cm.$^{-1}$ was found by Thompson and Torkington (*J.*, 1945, 640) to be intense with many esters and was assigned to a mode largely controlled by stretching of the C–O bond, although Francis has given arguments suggesting that it also involves some participation of the contiguous carbonyl group. Some years ago the intensity of this band near 1200 cm.$^{-1}$ in a series of esters was measured in this laboratory by Orr (Diss., Oxford, 1949), and we have recently repeated and extended his measurements. Since our results cover a wider range of compounds than was studied by Francis and reveal details not mentioned by him, an account is given below.

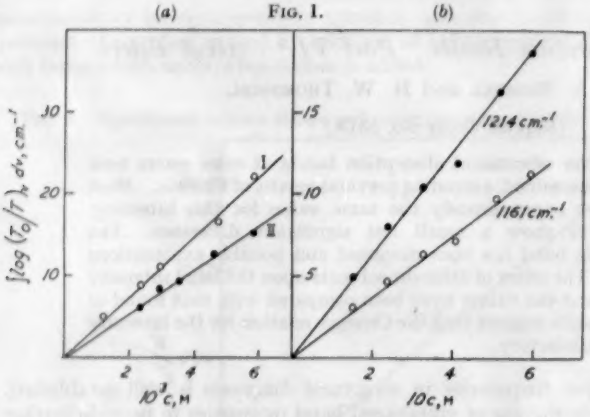
The band near 1200 cm.$^{-1}$ is not always single, but with many esters has at least two and probably more components. In formates, a close pair of bands lies between 1150 and 1220 cm.$^{-1}$, the components moving closer together as the alkyl chain lengthens. The band at lower frequency is usually the weaker, and its relative intensity falls in passing up the series. With acetates, there appears at first sight to be a single band, but closer inspection

* Parts I—V; *Proc. Roy. Soc.*, 1948, *A*, **192**, 498; *Trans. Faraday Soc.*, 1950, **46**, 103; *Proc. Roy. Soc.*, 1951, *A*, **208**, 332, 341; *ibid.*, 1954, *A*, in the press.

suggests another doublet, the higher-frequency component being very weak in methyl acetate but increasing in relative intensity along the series. In methyl propionate the split is clear, as also indicated by Francis, but with higher propionates the components are inseparable. Reference to the previous spectral charts shows that the separate components are clearly seen with butyrates and *iso*butyrates, and where higher alkyl radicals are present more than two bands may occur. The exact location of the bands is different for the different sets of homologues, and is only affected slightly by the solvent used.

For the band areas, $B' = \int \ln (T_0/T)_\nu \, . \, d\nu$, where T_0 and T denote the apparent transmitted energy as opposed to the true values I_0 and I and this was determined by graphical integration of the plots of $\ln (T_0/T)_\nu$ against ν. B' was determined for a series of concentrations (c) and the linearity of the plots of B' against c showed that extrapolation by the method of Wilson and Wells (*J. Chem. Phys.*, **1946**, **14**, 578) was not necessary. The slope of the plots gave B_0 and the true band intensity $A = (1/cl.) \int \ln (I_0/I)_\nu \, . \, d\nu$ was then given by B_0/l. The units used were: concentration in molecules per c.c., path length in cm., frequency in cycles per sec., with natural logarithms.

FIG. 1.



(*a*) Path length, 0·237 cm. I, *n*-Propyl acetate; II, ethyl propionate.

(*b*) Path length, 0·004 cm. Methyl formate.

We have measured the values of A for the " total " band near 1200 cm.$^{-1}$. Fig. 1(*a*) shows typical plots for *n*-propyl acetate and ethyl propionate, and the results are summarised in Table 1. Although no special procedure was used to apply wing corrections to the band areas (Ramsay, *J. Amer. Chem. Soc.*, **1952**, **74**, 72), the values given are probably reliable to $\pm 5\%$. Table 1 also includes Francis's results, and those of Orr,

TABLE 1. *Values of* 10^6A *in units cm.*^{2} *molecule*$^{-1}$ *sec.*$^{-1}$.

Substance	Francis (CCl_4)	Orr (MeCN)	Present work (CS_2)	Substance	Francis (CCl_4)	Orr (MeCN)	Present work (CS_2)
Methyl formate ...	—	147	130	*iso*Butyl acetate	—	—	176
Ethyl formate	—	170	169	*sec.*-Butyl acetate	—	—	187
n-Propyl formate ...	—	164	152	*n*-Amyl acetate ...	—	163	176
n-Butyl formate ...	—	176	165	Methyl propionate	129	116	126
*iso*Butyl formate ...	—	—	168	Ethyl propionate...	150	140	134
Methyl acetate	139	144	125	*n*-Butyl propionate	—	144	—
Ethyl acetate	176	166	165	*iso*Butyl propionate	—	—	149
n-Propyl acetate ...	177	164	180	*n*-Amyl propionate	—	140	—
*iso*Propyl acetate ...	—	—	170	Dimethyl carbonate	—	—	318
n-Butyl acetate ...	—	—	170	Diethyl carbonate	—	—	350

although the latter may be somewhat less accurate. The data show that for all the simple aliphatic monobasic acid esters about the same value is found for the intensity. However, the value for the methyl ester of an acid is significantly lower than for the higher

homologues. It is possible that with the propionates the intensity is lower than with acetates and formates by an amount which exceeds plausible experimental error. It should be noted that the values for the two alkyl carbonates are about twice that for an ester containing a single ester group. This might imply that the method could be used for determining the number of alkoxycarbonyl groups in a molecule, but this is not very likely, since apart from other considerations it may be difficult in more complex cases to identify the bands concerned. It is interesting that the resonance energy of carbonates (40—50 kcal./mole) is roughly double that of the simple alkyl esters (17—25 kcal./mole) (Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, 1939; Wheland, "Theory of Resonance," Wiley, New York, 1944), supporting the correlation of this property with the band intensity (Barrow, *J. Chem. Phys.*, 1953, **21**, 2008).

Now, with the formates it is possible to estimate the individual contributions of each of the "pair" of bands ν_a, ν_b near 1200 cm.$^{-1}$. Table 2 summarises the results found by

TABLE 2.

Solvent: acetonitrile

Values of A in cm.^{2} molecule^{-1} sec.$^{-1}$.

Substance	ν_a	10^8A	ν_b	10^8A	Total 10^8A
Methyl formate	1161	54·3	1214	92·5	147
Ethyl formate	1155	30·5	1195	140	170
n-Propyl formate	1154	25·6	1190	138·3	164
n-Butyl formate	1151	14·4	1186	162	176
Methyl propionate	1178	19·9	1208	96·1	116
Methyl acetate	1253	133	1288	10·6	144
Ethyl acetate	1249	(147)	1273	(19)	166
n-Propyl acetate	1246	(106)	1268	(58)	164
n-Amyl acetate	1246	(76·5)	1260	(86)	163

Orr, the results for methyl formate being shown in more detail in Fig. 1(*b*). With the acetates, the separation of the severely overlapping bands made the estimation of separate band areas (in parentheses in Table 2) somewhat artificial, although the trends are undoubtedly as indicated by the results. It would, of course, have been possible to select one or other of the "pair" of bands as due to the vibration concerned, and to infer that in formates the intensity varies steadily along a homologous series. The regularity of the values of the total band area suggests, however, that it is more reasonable to include the "total" band areas in all cases. Francis appears to do this in the case of methyl propionate.

We must, then, interpret the doubling of the band, or indeed the possibility that it may have several components. Thompson and Torkington (*J.*, 1945, 640) suggested that the C–O–R part of the alkoxycarbonyl group might have two vibrations connected with the C–O–C part of the skeleton. The somewhat anomalous result with methyl esters might support this hypothesis, as might also the rough equality of ν_a and ν_b with methyl formate.

An alternative interpretation would be to assume the occurrence of rotational isomers. Similar observations have been described by Jones, Humphries, Herling, and Dobriner (*J. Amer. Chem. Soc.*, 1951, **73**, 3215) for the 3-acetoxy-steroids, and they have explained them in this way. The investigation of rotational isomerism in esters by measurements of dipole moment has given only inconclusive evidence.

The effect of the solvent upon the relative intensities of the components of a "pair" should be mentioned. With methyl formate in acetonitrile the ratio of the molar extinction coefficients of ν_b and ν_a is about 1·2, whereas in carbon disulphide it is about 0·9. This effect might arise, however, from the effect of differences in bonding power of the solvents upon one component of the band pair if it involves participation of the carbonyl group.

Some measurements were carried out with methyl formate to compare its total band intensity at 1200 cm.$^{-1}$ in the gas phase and in various solvents. For the vapour a cell 10·3 cm. in length was used, and Fig. 2 shows the plot of B' against the partial pressure of vapour, dry air being added up to 1 atm. Table 3 gives the values for A_g and A_s. The effect of a dielectric medium of refractive index n upon the absorption by a dipole has been

TABLE 3. *Values of* A *in cm.*^{2} *molecule*$^{-1}$ *sec.*$^{-1}$ ($\log_e$).

Solvent	n_D	10^8A	A_s/A_g	Solvent	n_D	10^8A	A_s/A_g
Vapour	—	149	1·00	Benzene	1·497	146	0·98
Acetonitrile	1·342	159	1·06	Tetrachloroethylene ...	1·502	145	0·97
Methylene chloride ...	1·420	152	1·02	Carbon disulphide ...	1·624	130	0·87
Ethylene dichloride ...	1·442	149	1·00	Methylene iodide	1·738	117	0·79
Carbon tetrachloride ...	1·457	148	0·99				

considered by Debye (*Handb. Radiologie*, 1933, **6**, 69) and by Onsager (*J. Amer. Chem. Soc.*, 1936, **58**, 1486). They have suggested values for γ in the relation, $A_s = A_g\gamma^2/n$; γ is the ratio of the internal electric field on the solute molecule to the external field, and is given by one or other of the following expressions:

$$\gamma = (n^2 + 2)/3 \text{ (Debye)}; \quad \gamma = 3n^2/(2n^2 + 1) \text{ (Onsager)}$$

Fig. 3 shows how the ratio A_s/A_g would be expected to vary with the refractive index for each of the theories, and also the ratio actually measured in the present work. Although

FIG. 2.

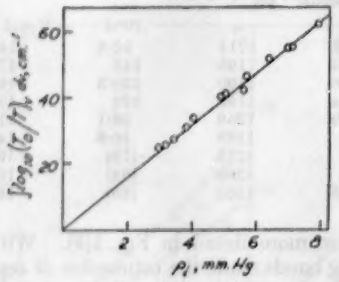
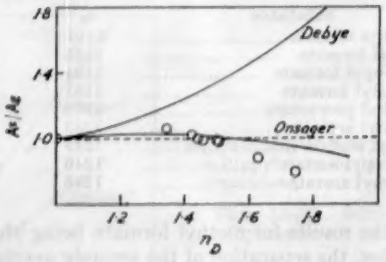


FIG. 3.



the measured values of A_s/A_g cannot be regarded as very precise owing to plausible errors of say 5% in the measured band areas, they indicate a surprisingly good agreement with Onsager's expression over a wide range. In any case the results show that alteration of solvent does not markedly affect the intensity of the band studied unless the refractive index is high. This result may be of general interest since few measurements of this kind seem yet to have been made.

Experimental.—The spectrometers used were a Perkin-Elmer 12C instrument, and a similar rock-salt prism spectrometer built in this laboratory. In both cases the effective slit widths were 3—4 cm.$^{-1}$, which is much less than the widths of the absorption bands. Scattered radiation errors were eliminated by means of a quartz shutter. Absorption cells were made in the usual way with rock-salt plates, and their thickness was determined from measured absorption bands of solutions by reference to a much thicker cell whose dimensions could be accurately measured. Solvents were purified according to Weissberger and Proskauer ("Organic Solvents," Oxford Univ. Press, 1935). The esters were repurified by fractionation and stored over anhydrous calcium sulphate.

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Intensities of Vibration Bands. Part VII. The* NH *Group.*

By R. A. Russell and H. W. Thompson.

[Reprint Order No. 5520.]

The integrated band areas of the fundamental stretching vibration band of the NH group in a number of types of compound have been determined, in order to correlate the band intensities with structural characteristics and the polar properties of this group. It has been found that marked differences occur between compounds of different classes, and in particular the intensities are very low with dialkylamines.

As part of a more general study of the intensities of vibration bands of polyatomic molecules we have measured the band associated with the fundamental stretching mode of the NH group in a variety of compounds. It was desirable in the first instance to limit the considerations to one key band, and primary amines containing the NH_2 group were therefore not examined since this group gives rise to a pair of bands differing in relative intensity in different circumstances. The compounds chosen included secondary amines, anilides, urethanes, and heterocyclic structures, and the object was to correlate the structural characteristics with the values of the integrated band areas A, the extinction coefficients $E_{max.}$ at the band peak, and the half band widths (band widths at half-peak optical density).

Two earlier sets of data are particularly relevant to our work. Bell (*J. Amer. Chem. Soc.*, 1925, **47**, 2192, 3039; 1926, **48**, 813, 818; 1927, **49**, 1837) measured the spectra of many amines in the liquid state, and in particular the bands near 3 μ of the NH and the CH group. There is little doubt that, with these compounds in the liquid state, hydrogen bonding of the NH group will occur, and Bell's results are therefore not strictly comparable with those for the free NH groups. Also, exact quantitative measures of the band intensities cannot be made from Bell's results. However, one important trend is noticeable in his data, namely, that in relation to the intensities of the CH bands, those of the NH groups in different molecules vary considerably. The strength of the NH band shows a general increase on passing from dialkylamines through the alkylanilines to diarylamines.

Wulf and Liddel (*J. Amer. Chem. Soc.*, 1935, **57**, 1464) measured the first overtone of the NH stretching mode and estimated band areas for amines, amides, and heterocyclic compounds containing this group. Their results again show significant variations of intensity from one compound to another, although at the time they suggested that the rough constancy of the band intensity might be used for approximate quantitative determination of the NH group. Some details of their work are discussed below.

Richards and Burton (*Trans. Faraday Soc.*, 1949, **45**, 874) determined the intensities of the NH fundamental stretching vibration band in methylaniline, ethylaniline, and diphenylamine. Although it is impossible to compare their results with ours on an absolute basis, there is rough agreement as regards the relative values for the different compounds.

Experimental

The substances were measured in dilute solution in carbon tetrachloride, although, as explained below, a few were also examined in the vapour phase. Each compound was purified by recrystallisation or fractional distillation. The spectra were recorded on a Perkin–Elmer 12C instrument with lithium fluoride prism, the calculated slit widths being about 10 $cm.^{-1}$ although the effective values were almost certainly rather greater than this. A quartz absorption cell 2·0 cm. thick was used. Several separate solutions of each compound were made up by weighing, and these were diluted as required. The concentrations generally used were in the region of 0·001M.

The apparent band areas $B' = \int \ln (T/T_0) \, . \, d\nu$ were determined by graphical integration. In determining these band areas there is the well-known difficulty of deciding the width in $cm.^{-1}$ over which integration shall be made. In general, here the extent of the wings measured was

* Part VI, preceding paper.

about eight times the apparent half-band width. It is possible that the values determined may be a few per cent too low (see Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72). Some plots of B' against c were satisfactorily linear, but others showed curvature. An extrapolation was carried out by plotting B'/cl against cl, the intercept giving A, the true band intensity. It is noteworthy that the plots of B' against cl which show appreciable curvature are for molecules which have a small value of the half-band width. The method of determining band areas takes into account the possibility of unsymmetrical band contour, any " hot " bands being included.

The apparent extinction coefficients $E^{a}_{max.} = (1/cl) \log (T/T_0)\nu_{max.}$ were also plotted as a function of cl, and a limiting value at $cl = 0$ was obtained by extrapolation. This value differs from $E^{t}_{max.}$, the true molecular extinction coefficient, in that it depends upon the slit width used. The apparent half-band widths (width at half-peak optical density) $\Delta\nu^{a}_{\frac{1}{2}}$ were also measured. These could only be estimated to about 0·5 cm.$^{-1}$, and in most cases appeared to vary little with concentration, *i.e.*, with optical density.

A few measurements were made on the dialkylamines and pyrrole with a Perkin–Elmer 21 double-beam spectrometer, a rock-salt prism being used.

Results and Discussion

Some typical results are shown in Figs. 1—4. The curvature of the plots of B' against cl might arise from several causes. One of these is the formation of hydrogen bonds between NH groups in different molecules. However, the concentrations used are very low and such association is unlikely. On the other hand, the deviation from linearity is most noticeable with those compounds in which the NH group may have a greater surplus positive charge on the hydrogen atom, such as the carbazoles. It is more probable, however, that the effect arises because the spectral slit widths used are in some cases a high fraction of the half band widths, which appear to be fairly small for the heterocyclic ring compounds and anilides.

The other important feature is the doubling of the NH bands with some compounds. The positions of these components (cm.$^{-1}$) are as follows (w = weak, m = medium, s = strong):

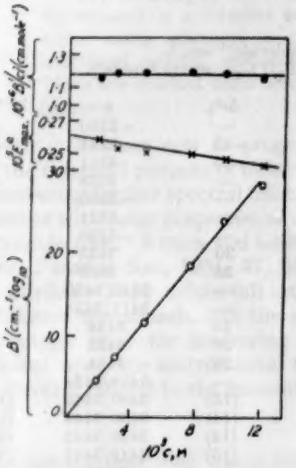
Acetanilide	3400 (w)	3442 (s)	Formanilide	3408 (m)	3434 (m)
p-Bromoacetanilide	3400 (w)	3445 (s)	*N*-Benzylaniline	3419 (m)	3450 (m)
α-Phenylacetanilide	3415 (s)	3441 (w)	*N*-Phenyl-α-naphthylamine	3417 (m)	3434 (m)
α-Phenylaceto-*p*-toluidide	3416 (s)	3442 (w)			

It is impossible to interpret either of the components with the anilides as being due to the harmonic of the carbonyl group fundamental, and it seems certain that both bands are connected with the NH group. The most probable explanation is that in all these cases rotational isomerism can occur, and the fact that there is a reversal of relative intensity between the components when a phenyl group is substituted in the acetyl group of anilides suggests that stereochemical considerations determine the preponderance of one form or the other. The total intensity of both bands has been taken as the measure of the NH group vibration, and if this is done all the results seem to fall into line.

The results are collected in the Table. As regards values of the intensity A, it can be seen that there are distinct groups. The alkylaryl- or diaryl-amines have values in the range 1·6—2·4, anilides and urethanes 2·7—3·9, and heterocyclic compounds 4·9—6·5. By contrast, the intensities for the dialkylamines are very much lower. The measurements were made in carbon tetrachloride, with which certain dialkylamines appear to undergo a slow chemical reaction, and there was consequently some suspicion that the apparent disappearance of the NH band was connected with this. The spectra of dimethylamine and diethylamine were therefore measured in the vapour phase, and compared with that of pyrrole vapour. Also, with the dialkylamines the intensity of the NH band is far smaller than that of the CH group bands, whereas the reverse is true for pyrrole. Rough measurement of the NH intensities in the vapour gave values agreeing with these found for the solution, but all the values for the dialkylamines must be regarded at present as approximate. There is in this case the possibility of some overlap with the much more intense CH bands. The weak nature of the NH band in the dialkylamines seems in agreement with Bell's results quoted above. Further, a similar result was found

by Marion, Ramsay, and Jones (*J. Amer. Chem. Soc.*, 1951, **73**, 305) when studying alkaloids containing a piperidine ring, although the band could be found with alkaloids containing indole nuclei or secondary amide groups. While the NH bands could not be found with solutions, they were detectable with the solid substances, where hydrogen bonds are formed and the polar character of the grouping will be affected. In this connexion

FIG. 1.



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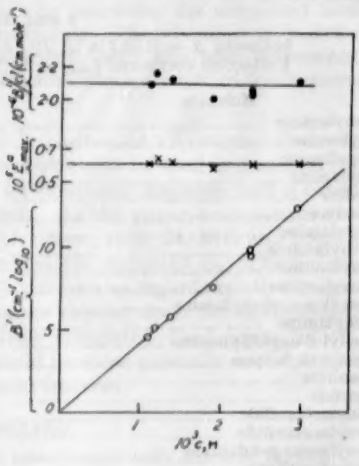

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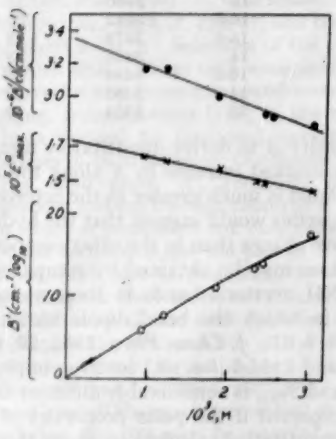
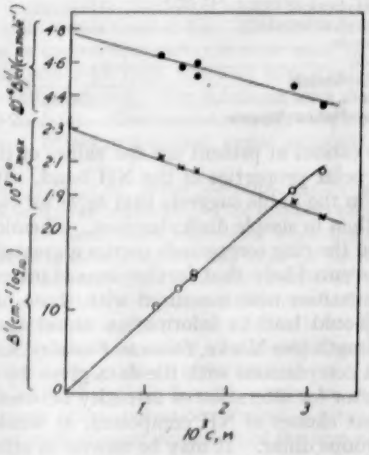


FIG. 4.



our result with 2-nitrodiphenylamine is significant. In this case there is internal hydrogen bonding of the NH group, and its vibration frequency falls to 3354. The band intensity is much higher than that for diphenylamine.

The extrapolated values of the extinction coefficients, namely $\underset{d\to 0}{\mathrm{Lt}}\ E^{e}_{max.}$, follow roughly the same trend as the band areas, and also fall into fairly clear groups. There are obvious objections to their use for analysis and diagnosis, however, since they are far more dependent on spectrometer characteristics than the band areas, and the wide variation in half-band widths of the different types of compound complicates the position further. In addition, when doubling of the band occurs the extinction coefficient of one peak is only

partially significant. In the Table the values in parentheses for anilides refer to the predominant component of the band pair, but no values are given for formanilide, *N*-benzylaniline, or *N*-phenyl-α-naphthylamine where the components have about the same intensity.

The different classes of compound also have characteristically different NH band widths. This is a matter for further discussion when more results are available for other absorption bands.

ν *and* $\Delta\nu^0_{\frac{1}{2}}$ *in cm.*$^{-1}$.

Intensity $A = (1/cl)f \ln (I_0/I)) \,.\, d\nu$ in cm.^{2} molecule^{-1} sec.$^{-1}$.
Extinction coefficient $E_{max.} = \lim_{cl \to 0} (1/cl) \log_{10} (T_0/T)_{max.}$ in cm.^{2} mole^{-1}.

Molecule	10^5A	$\Delta\nu^0_{\frac{1}{2}}$	ν	$10^{-4}E_{max.}$
Dimethylamine	~0·5	—	~3350	—
Diethylamine	~0·5	~45	3334	—
Dipropylamine	~0·5	~45	3311	—
Dibutylamine	~0·5	—	3338	—
Piperidine	~1·0	—	~3350	—
Morpholine	~1·0	—	3351	—
Dibenzylamine	~3·0	—	~3330	—
N-Methylaniline	16	30	3433	3·9
N-Ethylaniline	13·6	35	3422	2·6
N-Benzylaniline	18·3	—	3419/3450	—
N-Phenyl-α-naphthylamine	18·4	—	3417/3434	—
Diphenylamine	22·2	25	3434	5·9
N-Phenyl-β-naphthylamine	24	27	3435	6·4
ββ-Dinaphthylamine	24	29	3434	6·1
Formanilide	27	—	3408/3434	—
Acetanilide	28	(15)	3400/3445	(12·5)
p-Bromoacetanilide	29	(14)	3400/3444	(13)
α-Phenylacetanilide	38	(14)	3416/3442	(14)
α-Phenylaceto-*p*-toluidide	37	(15)	3415/3441	(13·3)
N-Phenylurethane	39	14	3446	17
1-Methylcarbazole	49	19·5	3482	18
2-Phenylindole	49	19	3480	18
3-Methylcarbazole	55	16·5	3482	22·5
Carbazole	55	18·5	3478	23
Pyrrole	57	14	3495	23·5
3-Methylindole	62	16·5	3490	25
Indole	65	14	3490	29
2-Nitrodiphenylamine	52	35	3354	10

We cannot at present use the values of the intensity A to derive quantitative measures of the polar properties of the NH bond. But the marked increase in A along the series shown in the Table suggests that $\delta\mu/\delta r$ for the NH bond is much greater in the heterocyclic bases than in simple dialkylamines. Chemical properties would suggest that the hydrogen atom in the ring compounds carries a greater positive charge than in the other compounds.

It seems likely that further important conclusions may be obtained by comparison of the intensities now measured with those of the NH overtone bands in these molecules. This should lead to information about the way in which the bond dipole varies with bond length (see Mecke, *Discuss. Faraday Soc.*, 1950, **9**, 61; *J. Chem. Phys.*, 1952, **20**, 1935). Rough comparisons with the data given by Wulf and Liddel (*loc. cit.*) for $2\nu_{NH}$ imply that the factor for alteration of intensity between ν_{NH} and $2\nu_{NH}$ is considerably different for the different classes of NH compound, as would be expected if the polar properties of their NH groups differ. It may be unwise to attempt quantitative calculations about this until the intensities for the overtones have been more carefully determined. The values given by Wulf and Liddel for the intensity of $2\nu_{NH}$ in dialkylamines are in marked contrast with those obtained by us for the fundamental, when compared with those for the other molecules, and the effect could only arise from a very significant difference in the nature of the NH bond in simple dialkylamines. Further work on this point is in progress.

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Intensities of Vibration Bands. Part VIII. The C≡N Group.*

By M. W. Skinner and H. W. Thompson.

[Reprint Order No. 5521.]

The intensity of the stretching vibration band of the C≡N group has been determined in a number of compounds by measuring the integrated band areas, using solutions in carbon tetrachloride. The vibration frequencies, half-band widths, and extinction coefficients have also been determined. There are marked variations in the intensities which are related to structural features.

Investigations are now in progress on the intensities of vibrational absorption bands with the threefold purpose of obtaining values which may be used in quantitative analysis, of discovering further spectral characteristics for structural diagnosis, and of correlating the intensities with polar properties of specific bonds. In this paper, some results are given for the cyanide link. Kitson and Griffith (*Analyt. Chem.*, 1952, **24**, 334) and Cross and Rolfe (*Trans. Faraday Soc.*, 1951, **47**, 354) determined the apparent extinction coefficients of some nitriles. Their values fall into line with our own as regards relative magnitudes for the different compounds, but the absolute values depend upon the characteristics of the spectrometer used for measuring them. True integrated band areas which are less dependent upon the instrumental factors should be more generally useful, and should be more directly related to the molecular structural features.

Experimental

The spectrometer used was a Hilger D209 instrument, with calcium fluoride prism and modified for single-beam operation, the spectra being recorded automatically. Wave-length calibration was carried out with rotation lines of deuterium chloride (Pickworth and Thompson, *Proc. Roy. Soc.*, 1953, *A*, **218**, 37) and the lines of the water band at 6 μ. The effective slit widths were about 6 cm.$^{-1}$. Solutions of the cyanides in carbon tetrachloride were used, in rock-salt absorption cells. Three cells were used, of thickness 0·53, 0·74, and 2·37 mm., a choice being necessary for any given compound according to its solubility. The solutions were made up by weighing, concentrations lying in the range 0·2—1·1M. The cyanides used were commercial products purified by fractional recrystallisation, or refractionation under reduced pressure, sometimes in an atmosphere of nitrogen.

The band areas, B', given by $B' = \int \ln ({}_0T/T)_\nu \,.\, d\nu$, were determined by graphical integration, and the limiting values of B'/cl at $cl = 0$ were obtained. This involves an extrapolation which is sometimes not very satisfactory. In some cases, especially when the apparent half-band width is large, the plot of B' against cl is closely linear, and there is no difficulty. However, this plot is frequently curved. The curvature may be the result of errors in determining the band areas, but it is usually most marked with compounds for which the half-band width is small, and when the effective slit widths are a high fraction of the latter quantity. In such cases the extrapolation of the values of B'/cl at small values of cl involves uncertainty. The values obtained cannot at present be regarded as accurate to more than about $\pm 5\%$.

The apparent half-band widths, *i.e.*, width at half optical density, were also measured. Since only small changes were noticed over the range of concentrations studied, a mean value is given below, but this must be regarded only as an approximate indication of the true half-band width.

In some cases, the main band due to the cyanide group stretching vibration near 4·45 μ was overlapped by other weak bands. The latter were taken into account in measuring the intensities.

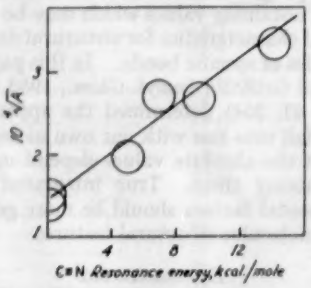
Results and Discussion

Table 1 summarises the values obtained. The compounds are seen to fall into fairly well-defined groups. The vibration frequency of the C≡N link in alkyl cyanides lies near 2250 cm.$^{-1}$, but conjugation with an aromatic ring, or the equivalent, lowers it to about 2230 cm.$^{-1}$. With the alkyl cyanides the intensities lie in the range $2{\cdot}0—3{\cdot}2 \times 10^{-6}$. All

* Part VII, preceding paper.

the aromatic nitriles have much higher values which depend upon the nature and position of substituents in the aromatic rings. It may be noted that, although in acrylonitrile and α-methacrylonitrile the vibration frequency is roughly the same as those in the aromatic cyanides, yet the intensity of the band is low and of the same rough magnitude as those of the aliphatic cyanides. Values are given in Table 1 also for hydrogen cyanide and deuterium cyanide, measured in the vapour state by Hyde and Hornig (*J. Chem. Physics*, 1952, **20**, 647), and for cyanogen chloride (Nixon and Cross, *ibid.*, 1950, **18**, 1316). The intensity found for *p*-methoxybenzonitrile is particularly high, and it seemed possible that this might arise accidentally because of overlapping with some overtone or combination band of the methoxy-group; for several reasons this is now regarded as improbable.

Barrow (*ibid.*, 1953, **21**, 2008) has tried to correlate the band intensity of the carbonyl group in different compounds with its resonance energy, and has found a rough parallelism



between A and the latter quantity; A is directly proportional to the quantity $(\delta\mu/\delta Q)$, the variation of molecular dipole moment with normal co-ordinate for the vibration. Values for the resonance energies of the cyanide link in some of the aromatic cyanides can be estimated as outlined by Wheland (" Theory of Resonance," Chapter 3, Wiley, New York, 1944) and by Barrow (*loc. cit.*). We thus obtain the results given in Table 2, and the plot

TABLE 1.

Values of $\Delta\nu_{\frac{1}{2}}$ and ν in cm.$^{-1}$. $A = (1/cl) \cdot \int \ln (I_0/I)_\nu \cdot d\nu$ in cm.^{2} molecule^{-1} sec.$^{-1}$. $E_{max.} = (1/cl) \log_{10} T_0/T)_{\nu max.}$ extrapolated to $cl = 0$, in cm.^{2} mole^{-1}.

Compound	10^5A	$\Delta\nu^{obs.}_{\frac{1}{2}}$	ν	$10^{-4}E_{max.}$	Compound	10^5A	$\Delta\nu^{obs.}_{\frac{1}{2}}$	ν	$10^{-4}E_{max.}$
Methyl cyanide ...	2·1	10	2251	1·33	α-Naphthonitrile	7·4	9	2222	6·5
Ethyl cyanide	2·4	11	2247	1·65	β-Naphthonitrile	11·5	9	2227	9·5
n-Propyl cyanide ...	2·5	12	2250	1·6	3-Cyanopyridine	5·4	12	2231	3·4
n-Pentyl cyanide ...	3·2	14	2244	1·75	Acrylonitrile	2·0	14	2231	1·5
Benzyl cyanide ...	2·5	14	2251	1·2	α-Methacrylonitrile	2·3	10	2227	1·65
Diphenylacetonitrile	2·5	13·5	2244	1·3	Allyl cyanide	2·2	19	2250	0·85
Benzonitrile	4·1	10·5	2229	2·5	Ethyl cyanoacetate	2·1	18	2260	0·87
o-Toluonitrile	7·6	10	2226	5·3	Hydrogen cyanide	0·075	—	2089	—
m-Toluonitrile	7·7	8	2229	6·6	Deuterium cyanide	1·33	—	1921	—
p-Toluonitrile	10·2	8	2229	10·5	Cyanogen chloride	8·4	—	2214	—
p-Methoxybenzonitrile	18·4	9	2226	16·5					

TABLE 2.

Compound	Resonance energy (kcal./mole)	$10^3\sqrt{A}$	Compound	Resonance energy (kcal./mole)	$10^3\sqrt{A}$
Methyl cyanide ...	0	1·41	*o*-Toluonitrile	7	2·75
Ethyl cyanide	0	1·55	α-Naphthonitrile ...	9·5	2·71
Benzonitrile	5	2·0	β-Naphthonitrile ...	14	3·35

shown in the Figure does in fact seem linear if the approximate nature of the values of the resonance energy is taken into account. For this purpose, it is assumed that the intensity in the gaseous phase is equal to that in carbon tetrachloride.

This preliminary survey suggests that it may be profitable to measure the band intensity for other substances containing the C≡N link. The narrow nature of the band also implies that better quantitative results may result from the use of still smaller effective slit widths of the spectrometer.

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Kinetics of a Polymorphic Transformation of Azoxybenzene.

By ARTHUR HODKIN and DUNCAN TAYLOR.

[Reprint Order No. 5789.]

A new monotropic polymorph of azoxybenzene has been characterised, and the kinetics of its transformation into the stable form under thin-film conditions have been investigated over the range 0—30°, a photometric method being used for the measurement of transformation rates. With highly purified material, the transformation is strictly linear with time, independent of film thickness, and relatively free from difficulties caused by spontaneous nucleation. The results agree well with the mechanism proposed by Hartshorne for polymorphic transformations, the energy of activation being 22·5 ± 1 kcal./mole (the heat of transition being assumed as 1 kcal./mole), and the temperature-independent factor very large. The activation energy agrees closely with 23 ± 1 kcal./mole, the heat of sublimation of the metastable form. The latter has been determined by an effusion method, the heat of transition being assumed to be as above. An approximate doubling of the rate after exposure to ultra-violet light is reported and discussed. The transformation is shown to parallel that of monoclinic ⟶ rhombic sulphur in several respects.

LITTLE is known of the mechanism of polymorphic transformations and few kinetic measurements of this type have been reported. The scarcity of data is due mainly to the difficulty of finding examples which undergo transformation in an easily measurable fashion. Experience with a polymorph of azoxybenzene (Campbell, Henderson, and Taylor, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 376) suggested that this might be a suitable case for study, and further work has revealed a second monotropic polymorph which is transformed into the stable modification in a manner eminently suitable for kinetic measurements. The results here presented lead to the same mechanism as that proposed by Hartshorne and his co-workers (*Discuss. Faraday Soc.*, 1949, **5**, 149; *J.*, 1951, 1097) for the monoclinic ⟶ rhombic sulphur transformation, *viz.*, one based on the difference in rates of escape of molecules from the two adjacent lattices, and requiring the full latent heat of sublimation of the metastable form as energy of activation.

EXPERIMENTAL AND RESULTS.

Preparation and Purification.—Azoxybenzene was prepared by sodium methoxide reduction of pure nitrobenzene and purified by crystallisation from aqueous methanol, followed by chromatography on a benzene–alumina column and a further crystallisation. These operations were carried out under red light owing to the ease with which the pale yellow azoxybenzene developed an orange colour when exposed to white light in contact with solvents (cf. Badger and Buttery, *J.*, 1954, 2243). Final purification was by distillation at a pressure $<10^{-6}$ mm. in a vertical tube (10″ × 1½″), also under dark-room conditions. The impure material in the bottom of the tube was kept molten by means of a water-thermostat at 50°, the lowest temperature at which a reasonable rate of distillation occurred, while the upper half of the tube was cooled to 10°. The condensate obtained during the first 12 hr. had a slight orange tint and melted over the range 35—36·2°. This material was completely removed from the tube, and

the second fraction collected during the next 24 hr.; it was very pale yellow, and its melting range was 35·6—36·4°. A third fraction, collected in the same manner, was again very pale yellow, but was contaminated with an unknown impurity which extended the melting range to 32—35·5°. All melting data were obtained at very slow rates of heating, a hot-stage microscope with high magnification and a calibrated thermometer being used. Without these stringent conditions, the difference between the first two fractions (apart from colour) would have been barely detectable, and indeed, under the same conditions several "AnalaR" standard substances rarely showed melting ranges of less than 0·5—1·0°. The second fraction was therefore considered to be very pure and was used in all kinetic and vapour pressure measurements.

Characterisation of the Polymorphs.—The polymorph described by Campbell, Henderson, and Taylor (*loc. cit.*) was readily obtained by cooling to 0° a liquid film of azoxybenzene held between a microscope slide and cover slip. It appeared as well-formed spherulites with brilliant polarisation colours and melted at 29°. This form is now designated III, the stable form being I. The transformation III ⟶ I occurred at a convenient rate at room temperature, but quantitative measurements with a travelling microscope were eventually abandoned, owing partly to a high degree of spontaneous nucleation, but mainly to the discovery of a further polymorph, designated II, whose transformation to I under thin-film conditions proved much more satisfactory. At a film thickness of 0·02 mm., form II showed a pale brownish-yellow colour under crossed Nicols, in contrast to the brilliantly coloured spherulites of III and the slightly less coloured needles of the stable form I. The final m. p. of II was 36·2°, only 0·2° less than that of the stable form. The transformation II ⟶ I was characterised by a slower rate than the III ⟶ I process, very little spontaneous nucleation, and a well-developed interface between the two forms. Furthermore, during the II ⟶ I transformation, the film became more opaque, and this fact was utilised in developing a photometric method for measuring the rate of the transformation (see below). No reversible transition points were observed and the relationship between the forms in all cases is therefore monotropic.

In view of the slight difference (0·2°) between the m. p.s of forms I and II, further characterisation of II was sought by means of *X*-ray powder photographs, using a Unicam 9-cm. camera with copper K_α radiation. Normally, the powdering of II would have resulted in its transformation to I before a satisfactory photograph could have been obtained. However, with the third fraction of azoxybenzene obtained in the vacuum-distillation, the transformation II ⟶ I was found to be almost completely inhibited, probably owing to some slight impurity, and a powder photograph of II could therefore be obtained. Photographs of I from fractions two and three were identical, while that of II was distinctly different from that of I. Spacings in Å are as follows:

Form I ...	9·01m	5·77w	5·36m	4·65s	3·86s	3·55m	3·22w	3·03m	2·70w	2·29w
Form II ...	8·41m	5·60w	4·58s	4·26s	3·78s	3·17w	3·05m			

(s = strong; m = medium; w = weak)

Density Determinations.—The densities of I and II (fraction three again being used), determined at 20° by flotation in water–sulphuric acid mixtures, were found to be 1·260 and 1·251, respectively.

Establishment of the Linearity with Time of the II ⟶ I *Transformation.*—In view of the higher density of form I, a small contraction away from the II—I interface may occur during the transformation, leading to a fall in rate with time (cf. Hartshorne *et al.*, *J.*, 1935, 1860; *J.*, 1938, 1636). A method of ascertaining whether or not the transformation remained linear with time was therefore necessary. A film of form II, 25 × 37 mm. and 0·025 mm. thick, was prepared between two microscope slides and seeded along one long edge with form I by scratching with a sharp point and painting with a slurry of form I in ethanol. Experiment showed that the use of this slurry had no effect on the transformation other than ensuring complete nucleation along the whole front. The film was kept at constant room temperature in diffused artificial light and photographed at 15-min. intervals, after which the negatives were projected with approximately 15-fold enlargement on to graph paper, and the successive II—I interfaces traced. The areas of transformation obtained in equal intervals of time for a fixed width of interface were cut out with a razor blade and weighed. Since the graph paper was of uniform weight per unit area, a relative measure of the rate of transformation was obtained from the weights of paper cut out. For two films, the transformation was found to be strictly linear with time.

Effect of Film Thickness.—A film was prepared as above with the addition that at one end the microscope slides were held apart with a piece of copper foil, thus producing a wedge shaped

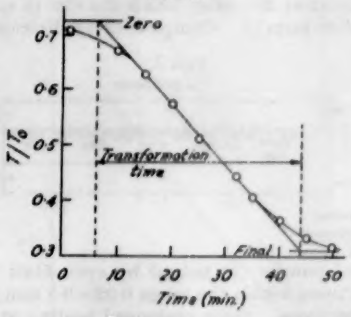
film varying from 0·002 to 0·095 mm. in thickness at right angles to the direction of growth, but of uniform thickness along any line parallel to the direction of growth. The transformation was photographed and traced on uniform graph paper as before. This tracing was then divided into three sections of equal width across the direction of growth, each section representing a different average film thickness, and the areas of transformation were cut out and weighed. All three sections showed the same constant rate of transformation. Furthermore, no correlation was ever found between film thickness and transformation rate as measured by the Spekker method described below.

Spekker Absorptiometer Method for measuring Transformation Rates.—Consider a rectangular film of azoxybenzene form II of uniform thickness and area a supported between glass slides. If the film is completely immersed in and at right angles to a uniform light beam of intensity I_0 per unit cross-section area and of total area a_0 ($a_0 > a$), then the total amount of transmitted light is

$$T = I_0(a_0 - a) + I_2 a - K$$

where I_2 is the intensity of the beam transmitted through unit area of the film, and the constant K allows for the light absorbed and scattered by the glass support. This equation may be simplified to $T = \text{const.} - a(I_0 - I_2)$. Let this film now be seeded along one edge with form I, and after times t' and t'' let areas a' and a'' respectively have been transformed to the

FIG. 1.



stable modification. Let I_1 be the intensity of the light transmitted by unit area of form I, and the total light transmitted at t' and t'' be T' and T'', respectively. Then

$$T' = \text{const.} - a'(I_0 - I_1) - (a - a')(I_0 - I_2)$$

and

$$T'' = \text{const.} - a''(I_0 - I_1) - (a - a'')(I_0 - I_2)$$

The rate of change of total light transmitted is

$$(T'' - T')/(t'' - t') = (a'' - a')(I_1 - I_2)/(t'' - t')$$

and is therefore a measure of the rate of change of area transformed. The latter, it should be noted, is a measure of the linear rate of advance of the interface only if the film is of uniform width perpendicular to the direction of growth, and provided no further nucleation occurs. Oblique growth of form I from " dark " regions of the film into the light beam would constitute further nucleation from the point of view of the theory. This was eliminated by having the film completely bathed in the beam in a lateral direction, and by the fact that spontaneous nucleation either along the edges or within the body of the film rarely occurred.

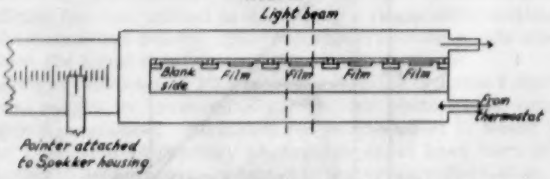
In using the Spekker instrument for rate measurements, it was balanced in the normal way with the solution position occupied by the transforming film, and the solvent position by a microscope slide. Thus at times t' and t'', values of T'/T_0 and T''/T_0 respectively were obtained by inverting the antilog of the drum reading, T_0 being the light transmitted by the blank slide. The rate of change of T/T_0 is $(a'' - a')(I_1 - I_2)/\{(t'' - t')T_0\}$ and is therefore directly proportional to the rate of transformation. Since the latter is constant at a given temperature, the plot of T/T_0 against time is a straight line, the gradient being proportional to the rate. A difficulty arises, however, if all the films do not have the same thickness, for this leads to variation in I_1 and I_2, and the rate of change of light transmitted would vary from film

to film even although the actual rate of transformation was the same for each. Furthermore, owing to irregularities in the advancing front, the whole of the front does not enter or leave the beam simultaneously and causes the T/T_0–time graph to be curved at the beginning and end of the measurements. These troubles were eliminated by extrapolating the central linear portion of the graph to the zero and final values of T/T_0 (see Fig. 1). The latter can easily be measured if the direction of growth is vertical and the film extends a few mm. above and below the vertical limits of the beam. From the extrapolation, the time required for that part of the film totally immersed in the light beam to be transformed completely is obtained.

A further requirement is that the light beam should be of uniform intensity along the direction of growth, otherwise a linear rate of transformation would not result in a linear change in the amount of light transmitted. Since photographs showed the Spekker beam to be of uniform intensity along its vertical axis in the slide position, experiments were always carried out so that the front advanced from the bottom to the top of the beam.

Preparation of Films and Measurement of Rates of Transformation.—Films of form II were prepared between microscope slides and cover slides 25 mm. long by 11 mm. wide, the corresponding light beam dimensions being 14 × 12 mm. The measured transformation times therefore corresponded to a 14-mm. advance of interface and a transformed area of 14 × 11 mm.^{2}. Under red-light conditions, a small quantity of powdered azoxybenzene was melted between a slide and cover slip at 40° on an electrically heated aluminium block, care being taken to exclude air bubbles. The slide was then cooled for 5 min. on a plane horizontal brass surface kept by thermostat at 20°, after which the film of supercooled liquid was seeded along its lower 11 mm. edge with form II. Complete crystallisation occurred in less than 2 sec.

FIG. 2.



By using the same volume of powder (as judged by eye), films were readily obtained, with practice, having uniform thickness within the range 0·02—0·1 mm., for which, as shown above, the rate is independent of thickness. Since prolonged heating at 40° caused some increase in rate, the heating was limited to 1·5 min. for a first melt and 0·5 min. for a second. Only first and second melts were used in the quantitative work, even although no detectable increase in rate occurred after three melts. The same lower edge was now scratched with a sharp point and painted with a slurry of form I in ethanol. Occasionally, transformation of the slight crust along the vertical sides of the film was more rapid than transformation within the body of the film, causing side nucleation and therefore non-linear plots of T/T_0 against time. This tendency was minimised by terminating the scratch 1 mm. from each end of the edge. This procedure for preparing films had to be rigidly adhered to, otherwise considerable variation in rate occurred. Even so, rates varied appreciably from one preparation to another, and accordingly a single middle fraction was used in all measurements.

The films were now transferred to the inner compartment of the double Perspex box shown in plan in Fig. 2. This box was mounted on a brass slide of the same cross-section as that which normally carried the cell-holder, and thus with the aid of the pointer and scale any one of the four films or the blank slide could be positioned accurately in the light beam. Experiments were carried out at 5° intervals between 0° and 30°, water or an ethylene glycol–water mixture being used as thermostat fluid. For measurements at or below 10°, the Spekker instrument was totally enclosed within a dry box provided with suitable windows and port-holes. Measurements below 0° were impossible owing to cracking of the films, and above 30° owing to nucleation difficulties. Red filters (Hilger No. 603) were used on the Spekker absorptiometer so that no wave-length shorter than 6000 Å reached the films.

Results for Measurements in Red Light.—The results for a typical exeriment at 25° are given in Fig. 1 and show that the requirements of the theory given above were adequately fulfilled. In the Table are given the arithmetic mean rates, expressed as 10^3 × (transformation time in min.)$^{-1}$, together with the number of experiments on which the mean is based, the standard deviation, and the coefficient of variation. The graph of $\log_{10}$ (Rate) against the $1/T$ is given

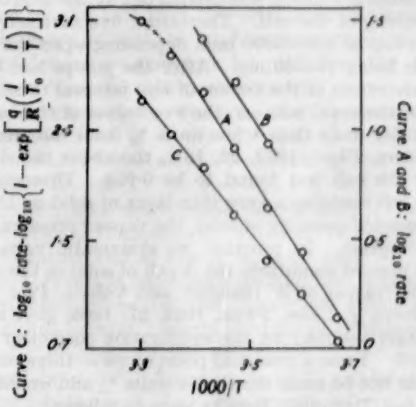
in Fig. 3, line *A*. By statistical calculation using regression equations (Weatherburn, "First Course in Mathematical Statistics," Cambridge Univ. Press, 1945) and omitting the 30° point, the equation for *A* was shown to be $\log_{10}(\text{Rate}) = -3932/T + 14{\cdot}55$, from which an apparent

Rates of transformation.

Temp.	0°	5°	10°	15°	20°	25°	30°
Red light conditions							
Rate	1·390	2·778	4·422	8·180	14·80	21·89	31·33
No. of expts.	16	14	12	19	28	27	22
Standard deviation (*S*)	0·124	0·181	0·358	0·532	2·74	5·10	3·57
Coeff. of variation (*S*/Rate)	0·089	0·065	0·081	0·065	0·185	0·233	0·114
After pre-irradiation with ultra-violet light.							
Rate	—	—	8·49	16·44	25·55	—	—
No. of expts.	—	—	12	18	15	—	—
Standard deviation (*S*)	—	—	0·855	1·67	3·44	—	—
Coeff. of variation (*S*/Rate)	—	—	0·101	0·102	0·135	—	—

activation energy of 17·9 kcal. (standard deviation 0·45) was obtained on the assumption (see p. 496) that the rate of the transformation can be represented by an Arrhenius-type equation. The 30° point was omitted from the calculation because it was shown to lie more than three

FIG. 3.



standard deviations below the calculated line through the other six points, thus indicating a slight curvature at the high-temperature end of *A*.

Influence of Pre-irradiation with Ultra-violet Light on Rate of Transformation.—Variations in rate up to 100% in the early stages of the work were found to be due to exposure of the films (prepared under otherwise standard conditions) to bright daylight. Semi-quantitative experiments at 20° showed that irradiation of form II films with a Hanovia ultra-violet lamp at a distance of 30 cm. before seeding with form I, followed by transformation in red light, gave increased rates up to *ca.* 100% after 5 minutes' irradiation, with no further increase up to 10 minutes' irradiation. On re-melting and re-transformation of the films without further irradiation, the rates tended to return to normal red-light values. This tendency was greater the shorter the period of irradiation. If the irradiation was carried out with the films in the liquid state (*i.e.*, before being seeded with form II), 10 seconds' exposure was sufficient to cause the maximum increase in rate (again *ca.* 100%). In this case the effect was more permanent, several re-melts and re-transformations being necessary before any noticeable decrease in rate occurred. Quantitative measurements were carried out at 10°, 15°, and 20°, the films being prepared in the same manner as for the red-light work, with the addition of 15 seconds' irradiation before seeding with the metastable form. Experiments below 10° were impossible owing to cracking of the films on cooling, and above 20° owing to difficulty of securing complete nucleation with form I at all points simultaneously along the lower edge of the films. Results are given in the Table and plotted in Fig. 3, line *B*. In view of the small number of points, little confidence can be attached to the slope of line *B*, but the indication is that no change in apparent activation energy occurs after irradiation.

Temperature Rise at the II–I *Interface during Transformation.*—Calculated by Hartshorne and Roberts's procedure (*J.*, 1951, 1097), the temperature rise at the interface was found to be of the order 0·03°, reasonable values for the specific heat and thermal conductivity of azoxybenzene being assumed by comparison with other organic compounds. This rise is very little more than the variation in the temperature of the thermostated Perspex box, and would have no significant effect on the rate measurements.

Vapour-pressure Measurements and Heat of Sublimation of Form I.—Vapour pressures were determined by Knudsen's effusion method (*Ann. Physik*, 1909, **29**, 179), a cylindrical brass effusion cell closed with a platinum foil diaphragm soldered to a screw-on lid being used. The construction was such that the azoxybenzene was contained within a perfect cylindrical volume 9·52 mm. long and of 4·76 mm. radius, the axially placed orifice in the 0·014-mm. thick platinum foil being 0·905 mm. in radius. During effusion in a vacuum better than 5×10^{-6} mm., the cell was contained in a vertical copper tube, 3″ long by 1″ in diameter, fused at the upper end to a B34 Pyrex joint and closed at the lower end by a copper disc brazed on to the tube. The lower end of the tube contained a Wood's metal plug fused to the copper and having a cylindrical recess which was a close fit to the effusion cell. The latter was thus in good thermal contact with the water thermostat surrounding the copper tube, the top of which was 2″ below the surface of the water. The minimum distance between the cell and the cold surface of a liquid-oxygen trap connected to the Pyrex joint was 8″. The same material (well ground) being used as for the kinetic measurements, effusion was carried out at the desired temperature for several hours before the first weighing of the cell. Thereafter, five successive weighings were carried out after effusion for intervals of 400—3000 min. depending upon the vapour pressure, the loss in weight in any intervals being 10—30 mg. After the pumps had been switched on, 5 min. elapsed before the commencement of the timing of any interval to allow the pressure to fall to $<10^{-3}$ mm. Calculated in the usual manner, the five values of the vapour pressure at any one temperature did not differ by more than a few units % from the arithmetic mean value. By Whitman's method (*J. Chem. Phys.*, 1952, **20**, 161), the above cell dimension being used, the probability factor W for the cell was found to be 0·959. Theoretically this value of W is applicable only when the cell contains a very thin layer of solid on the bottom, and if the cell initially contains an appreciable quantity of solid, the vapour pressure should show an apparent decrease as the cell is emptied. In practice, no systematic variation was ever observed, indicating that under the present conditions the depth of solid in the cell was not an important factor. An alternative derivation of W (Bradley and Volans, *Proc. Roy. Soc.*, 1953, *A*, **217**, 515; Rossman and Yarwood, *J. Chem. Phys.*, 1953, **21**, 1406) gave a value between 0·95 and 1·0, depending on the values assumed for the evaporation coefficient and the effective area of the solid in the effusion cell. From a practical point of view, therefore, errors due to the use of the Whitman figures would not be more than a few units % and would have very little influence on the slope of the $\log_{10} p$–$1/T$ graph. Results were as follows:

Temp.	19·2°	23·2°	27·2°	31·2°	35·2°
Vapour pressure $\times 10^4$, mm. Hg	0·735	1·26	2·11	3·71	6·08

Calculation by use of regression equations showed that the vapour pressure (in mm.) can be represented by $\log_{10} p = -5201/T + 13{\cdot}66$, which leads to 23·7 kcal./mole for the heat of sublimation, with a standard deviation of 0·3 kcal.

To check the accuracy of the measurements, the vapour pressure of benzophenone (for which accurate values are known; Neumann and Völker, *Z. physikal. Chem.*, 1932, *A*, **161**, 33; Hartshorne and Bradley, personal communication) was determined over the same pressure range. The material used (B.D.H.) was crystallised from ethanol followed by vacuum-sublimation as for azoxybenzene, and had a melting range 47·9—48·2°. The measured vapour pressures, together with Neumann and Völker's values, were as follows:

Temp.	9·0°	17·0°	21·4°	25·3°
Observed v. p. $\times 10^4$ (mm. Hg)	0·74	2·24	3·92	6·04
Neumann's value $\times 10^4$ (mm. Hg)	0·71 *	2·14	3·89	6·46

* Extrapolated value.

The discrepancies are considered to be slightly greater than the experimental error, and indicate that the value of W should be a few units % higher than the Whitman figure in order to reduce the lower values, and that slight self-cooling occurred at the highest pressure. By using an effusion cell of the same dimensions but smaller orifice (radius 0·518 mm., Whitman W 0·976)

the vapour pressure at 25·3° was found to be $6{\cdot}51 \times 10^{-4}$ mm., which supports the suggestion of self-cooling at this pressure with the larger-orifice cell. However, if the above results are used to calibrate the larger-orifice cell, the corrected azoxybenzene values lead to a heat of sublimation not greater than 24·9 kcal./mole, only 1·2 kcal./mole greater than that obtained when using the Whitman value of W. The heat of sublimation can therefore be given with confidence as 24 ± 1 kcal./mole. Measurements on liquid azoxybenzene between 37° and 49° gave $\log_{10} p$ (mm. Hg) $= -4361/T + 10{\cdot}97$, corresponding to a heat of vaporisation of 19·9 kcal./mole (standard deviation 0·13), and therefore a heat of fusion of *ca.* 4 kcal./mole.

Discussion

Transformation under Red-light Conditions.—The transformation form II ⟶ form I, in view of its strict linearity with time, independence of film thickness, and the occurrence of only slight spontaneous nucleation, has proved very satisfactory for kinetic measurements near room temperature under thin-film conditions. The average coefficient of variation of the rate is 11·7% (*i.e.*, on the basis of a rate = 100), a comparable figure in the sulphur work (Hartshorne, personal communication) being 11%, and can be considered good for this type of kinetic work. The low variance is considered to be due to (*a*) the high purity of the azoxybenzene, (*b*) the carefully standardised procedure for preparing and transforming the films, and (*c*) the fact that the total area of transformation at any one temperature was relatively large (about 30 cm.^{2} as compared with about 4·5 cm.^{2} for sulphur). Reasonable confidence can therefore be placed in the activation energy and pre-exponential factor derived from the rate measurements.

On the basis of an Arrhenius-type equation, the apparent activation energy is 17·9 kcal./mole (Fig. 3, line *A*). This is significantly less than the heat of sublimation of form II, *viz.*, 23 ± 1 kcal./mole, obtained on the reasonable assumption of 1 kcal./mole for the heat (q) of the transition II ⟶ I: cf. $q = 0{\cdot}7$, 1·4, and 1·5 kcal./mole for benzophenone, carbon tetrabromide, and *n*-undecane respectively (Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier, 1950). However, the indicated curvature at the high-temperature end of line *A* suggests that the expected maximum in the rate (observed with sulphur) might have been realised had it been possible to carry out rate measurements at temperatures nearer the theoretical transition point (T_0), which occurs above the m. p. of either form and where the rate of transformation would be zero. In view of the closeness of the m. p.s of the two forms, T_0 would probably occur at a temperature not higher than about 50°. An estimate of T_0 can be obtained as follows, the units of the vapour pressure p being mm. Hg. The equation for the solid–vapour curve of form I is $\log_{10} p = -5201/T + 13{\cdot}66$, and if it is assumed that $q = 1$ kcal./mole, the corresponding equation for form II is therefore $\log_{10} p = -4976/T +$ constant. The vapour pressure of form II at its m. p. (36·2°) can be obtained from $\log_{10} p = -4361/T + 10{\cdot}97$, the equation for the liquid–vapour curve, and hence the value of the constant found to be 12·95. The two solid–vapour curves can now be shown to intersect at 44°, which is the value of T_0. This value, in view of the small value of q, is subject to appreciable error, but the calculation does show that $q = 1$ kcal./mole is consistent with a value of T_0 between 40° and 50°. It is of interest therefore to consider the results for the present monotropic process in the light of the mechanism proposed by Hartshorne for the enantiotropic sulphur transformation. The latter is based on the difference in rates of escape of molecules from the two adjacent lattices and leads to the equation

$$\log_e \text{Rate} - \log_e\{1 - \exp[q(1/T_0 - 1/T)/R]\} = -E/RT + \log_e \tfrac{1}{2}A$$

where E and A are respectively the activation energy of escape and the temperature-independent factor of the rate of escape of molecules from the metastable lattice. In the case of sulphur, the plot of the left-hand side of the equation against $1/T$ did not give the required straight line except in the temperature range 0—30°, the corresponding value of E being close to 22·5 kcal./mole, which is the accepted value of the heat of sublimation of monoclinic sulphur. Hartshorne has shown, however, that over the whole range of measurements (0—80°) the deviations from the requirements of the theory can be accounted

for by quite small variations in the activation energy of escape of molecules from the stable lattice. Applied to the present results, with $q = 1$ kcal./mole and $T_0 = 50°$ C, the above equation gives line *C* in Fig. 3, the slope coresponding to $E = 22{\cdot}5$ kcal./mole, which agrees well with **23** $\pm$ 1 kcal./mole, the heat of sublimation of form II. Variation of q from 0·5 to 2·0 kcal./mole or of T_0 from 50° to 40° C does not alter the value of E by more than 1 kcal. or substantially affect the fit of the points to a straight line. The value of A, calculated at 20°, is $7{\cdot}72 \times 10^{14}$. Theoretically, if application of Hartshorne's equation does in fact yield a straight line for *C* in Fig. 3, then line *A* should be slightly curved over its entire length. The curvature required (found by mathematical transformation of *C* back to *A*) is, however, very slight and the resulting curve is indistinguishable within the experimental error from the straight line *A*. Over a larger temperature range, the curvature would probably be more apparent as it is with sulphur. The same conclusion regarding activation energy was reached by Hartshorne *et al.* for *o*-nitroaniline (*J.*, 1935, 1860), but not for mercuric iodide (*J.*, 1938, **1636**) where the activation energy was less than the heat of sublimation.

Calculations based on work by Burgers (*Proc. K. Ned. Akad. Wet.*, 1947, **50**, 719) and Mott (*Proc. Phys. Soc.*, 1948, **60**, 391) have shown (Hartshorne, *Discuss. Faraday Soc.*, 1949, **5**, 149) that for sulphur the thermal activation of one molecule with energy equivalent to the heat of sublimation leads to the transformation of *ca.* 10^7 molecules. By the same procedure, with use of the above value of *A*, or by application of the Polanyi–Wigner equation, the results for azoxybenzene give a value of *ca.* 10^9. This number of molecules corresponds to a unit of volume of *ca.* 3×10^{-13} cm.^{3}, which is within the range of the estimated size of a mosaic block. Hartshorne (*loc. cit.*; cf. Garner, *ibid.*, p. 194) has interpreted this behaviour on the basis of a mosaic block theory. It is thought that the transformation occurs with low energy of activation over small elements of volume (*i.e.*, mosaic blocks) and that a much higher energy is required to " bridge " adjacent blocks. If the bridges are formed by condensation of molecules from the vapour phase, the higher energy of activation will be approximately equal to the heat of sublimation and will determine the temperature coefficient of the transformation.

Further parallels to the sulphur transformation are as follows: (*a*) although the average rate of interface advance was constant under given conditions, microscopic examination showed that the transformation proceeded spasmodically over short distances, caused no doubt by lattice discontinuities of one kind or another, and that growing stable crystals did not change their orientation when crossing boundaries between differently oriented metastable crystals; (*b*) an estimate by Hartshorne's method (*J.*, 1951, 1113) of the vibration frequency of molecules from which bridges between mosaic blocks are formed was 10^5—10^6 times greater at 20° than the usual frequency of *ca.* 10^{13} sec.$^{-1}$ (with sulphur the discrepancy at 0° is 10^4 times); (*c*) from the vapour-pressure data, the rate of evaporation at 20° can be shown to be 10^5—10^6 times greater than that calculated from the Polanyi–Wigner equation: the corresponding discrepancy for rhombic sulphur is *ca.* 10^4 (*loc. cit.*).

Transformation after Irradiation with Ultra-violet Light.—The approximate doubling of the rate of the II ⟶ I transformation after irradiation with ultra-violet light could be due to either a reduction in the activation energy of *ca.* 500 cal./mole, a quantity which is too small to be detected in the present instance (cf. Fig. 3) or an approximate doubling of the effective volume of the mosaic blocks. The fact that the increase in rate is more pronounced when irradiation is carried out with the films in the liquid rather than the solid state, suggests that the primary cause is a photochemical one. Since it is known (Badger and Buttery, *loc. cit.*) that irradiation by sunlight of azoxybenzene in organic solvents slowly leads to the formation of *o*-hydroxyazobenzene, it seems likely that minute amounts of this compound would be produced during the 15-sec. ultra-violet irradiation. Incorporation of the hydroxy-compound in the lattice of form II may then have been such as to influence the physical state of the films and favour the bridging of lattice discontinuities. In this connection, it has been observed that (*a*) red-light films, after being " annealed " at room temperature in the dark for 18 hr., were transformed at a much slower rate than normal, and (*b*) if the transition III ⟶ II preceded the II ⟶ I process

in an otherwise standard red-light film, the II ⟶ I rate was much greater than normal. Both observations show that the physical state of the films had an important influence on the rate of transformation. However, attempts to reproduce the acceleration effect with known mixtures of azoxybenzene with *o*-hydroxyazobenzene failed. The destruction of the effect on frequent remelting of the films suggests, on the other hand, that the active photochemical product may be *cis*-azoxybenzene, which would revert to the normal form on melting (cf. *cis*-azo-compounds; Campbell, Henderson, and Taylor, *J.*, **1953**, 1281). However, the existence of *cis*-azoxybenzene has not yet been established unambiguously (Gehrckens and Müller, *Annalen*, **1933**, **500**, 296).

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Stages in Oxidations of Organic Compounds by Potassium Permanganate. Part VI. Oxidations of Ketones and of Pyruvic Acid.*

By ALAN Y. DRUMMOND and WILLIAM A. WATERS.

[Reprint Order No. 5566.]

Aliphatic ketones are attacked by manganic pyrophosphate only after enolisation. With *cyclo*hexanone, under nitrogen, the enolisation rate, measured in mole $l.^{-1}$ $hr.^{-1}$, equals the limiting oxidation rate, measured in equiv. $l.^{-1}$ $hr.^{-1}$, and since the addition of vinyl cyanide, which then polymerises, does not affect the oxidation rate it is suggested that the initial organic radical rapidly disproportionates. Oxidation commences at the α-CH groups of ketones and eventually leads to very extensive degradation, though 2-hydroxy*cyclo*hexanone is much less rapidly oxidised than *cyclo*hexanone itself. Oxygen can combine with the organic radicals that are generated, and affects both the rate and the mechanism of the oxidations.

However, pyruvic acid, which is oxidised quantitatively to acetic acid and carbon dioxide, reacts by first forming a chelated manganic complex, enolisation not being involved.

IN Part II of this series (*J.*, **1953**, **440**) it was indicated that both aldehydes and ketones were oxidised by manganic salts, and that with the former the rate-determining stage was that of their acid-catalysed enolisation. Kinetic studies of some ketone oxidations have now been made; the oxidations of *cyclo*hexanone and of pyruvic acid have been examined in detail and comparative measurements have been made with a number of other aliphatic ketones.

It now seems that, as with the aldehydes, simple ketones, are oxidised by manganic pyrophosphate only after enolisation, though in the case of pyruvic acid, with which cyclic complex formation may be postulated (compare 1 : 2-glycols, Part III, *J.*, **1953**, 3119; and malonic acid, Part IV, *J.*, **1954**, **2456**), enolisation does not seem to be necessary. In this respect oxidations by manganic salts resemble corresponding oxidations by ceric salts (Shorter and Hinshelwood, *J.*, **1950**, **3275**; Shorter, *J.*, 1950, 3425; Fromageot, *Compt. rend.*, 1926, **182**, 1411; *Bull. Soc. chim.*, 1926, **39**, 1207), though these workers did not notice that oxygen affected the mechanism of the reaction. Oxidation of ketones *via* enolisation has also been proposed for reactions with permanganate (Lejeune, *Compt. rend.*, 1926, **182**, 694), chromic acid (Petit, *Bull. Soc. chim.*, 1945, **12**, 568), and alkaline ferricyanide (Speakman and Waters, *J.*, 1955, 40). Consequently, the reaction mechanism deduced below for the oxidation of *cyclo*hexanone may represent the general route by which ketones are oxidised by electron-abstracting reagents.

Oxidation of cyclo*Hexanone and of Diethyl Ketone.*—(1) *Kinetic studies in the absence of*

* Part V, *J.*, 1955, 217.

oxygen. The oxidation of aqueous solutions of *cyclo*hexanone by acid manganic pyrophosphate, under nitrogen, is initially a strictly first-order reaction with respect to the ketone (see Table 5). The initial rate increases with increasing acidity of the solution as shown in Fig. 1, and varies with Mn^{III} concentration as shown in Fig. 2 (curve *A*), reaching a limiting value at quite moderate concentrations of the oxidiser. This limiting rate, measured in equivs. per l., is identical with the corresponding rate of enolisation of *cyclo*hexanone measured, by the well-known iodination method, in moles per l. (see Table 1). Consequently, at quite moderate concentrations of the oxidiser, the measurable acid-catalysed formation of the enol [this is the forward reaction (2); see Bell, Lidwell, and Wright, *J.*, 1938, 1861; Zucker and Hammett, *J. Amer. Chem. Soc.*, 1939, **61**, 2785]

TABLE 1. *Oxidation and enolisation rates of* cyclo*hexanone at 25·0°.*

pH	1·50	1·10	0·50
$-d[Mn^{III}]/dt$ (equiv. $l.^{-1}$ $hr.^{-1} \times 10^{-6}$)	3·04	5·58	8·16
$+d[Enol]/dt$ (mole $l.^{-1}$ $hr.^{-1} \times 10^{-6}$)	2·97	5·41	8·51

Each mixture initially contained $3·53 \times 10^{-2}$M-*cyclo*hexanone and 0·137M-pyrophosphate. The initial concentrations of Mn^{III} and iodine were $1·65 \times 10^{-4}$M and $9·31 \times 10^{-3}$M, respectively, in the two sets of experiments. The catalytic, and salt, effects due to ions and molecules were thus the same in each case.

becomes rate-determining: the velocity of reaction (3) affects the rate at low Mn^{III} concentration only:

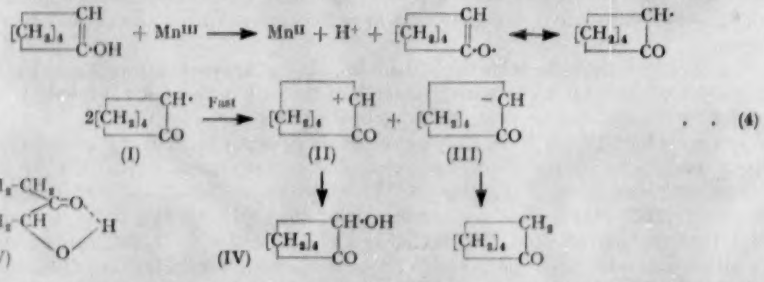
$$R{\cdot}CH_2{\cdot}CO{\cdot}R' + H^+ \rightleftharpoons R{\cdot}CH_2{-}\overset{+}{C}(OH){-}R' \text{ (immediate)} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$R{\cdot}CH_2{-}\overset{+}{C}(OH){-}R' \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} R{\cdot}CH{=}C(OH){-}R' + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$R{\cdot}CH{=}C(OH){-}R' + Mn^{III} \xrightarrow{k_3} Mn^{II} + \text{Radical} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Reaction (3) is not reversible, since manganous salts have no effect on the reaction velocity, but the complexity of the relation between oxidation rates and pH shows that k_3 does to some extent depend upon the redox potential of the manganic complex which is concerned. At high acidities the predominating factor seems to be the rate of the general acid catalysis of the enolisation; at low acidities the greatly reduced oxidising power of the manganic pyrophosphate can be noticed.

In the oxidations of aldehydes (Part II, *loc. cit.*) and of pinacol (Part III, *loc. cit.*) with manganic pyrophosphate the free radicals formed by the one-electron-removal process corresponding to (3) are rapidly oxidised by a second equivalent of Mn^{III}, and with malonic



(4)

acid (Part IV, *loc. cit.*) this second stage of the oxidation does not affect the overall reaction rate. With *cyclo*hexanone, however, the addition of vinyl cyanide to the oxidising system, though it leads to the formation of poly(vinyl cyanide) containing ketonic end-groups, as shown by infra-red spectra, does not affect the rate of destruction of Mn^{III}. Hence the organic radicals which are formed (*e.g.*, I) cannot be oxidised very rapidly by more manganic salt. Since at high Mn^{III} concentrations the enolisation rate (2) equals that of destruction

FIG. 1.

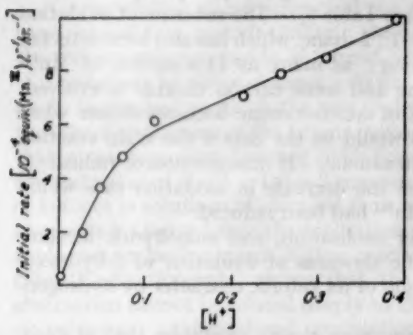


FIG. 2.

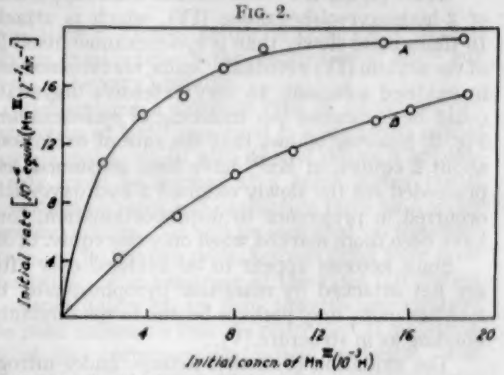


FIG. 1. *The effect of* [H^+] *on the rate of oxidation of* cyclo*hexanone.*

Temp. 25·0°; [Pyrophosphate], 0·152M; initial concns. (M × 10^{-3}): [Mn^{III}], 1·84; [ketone], 1·96.

FIG. 2. *The variations of the rates of oxidation of* cyclo*hexanone (curve A) and diethyl ketone (curve B) with increasing concentration of manganic pyrophosphate.*

A, Temp. 25·0°; pH 1·53; [Pyrophosphate], 0·153M; [*cyclo*Hexanone], 1·96 × 10^{-2}M.
B, Temp. 30·0°; pH 0·93; [Pyrophosphate], 0·176M; [Diethyl ketone], 4·02 × 10^{-2}M.

FIG. 3.

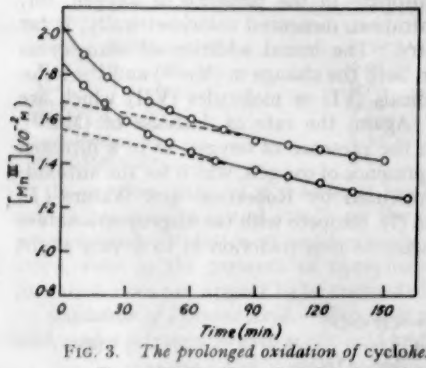


FIG. 4.

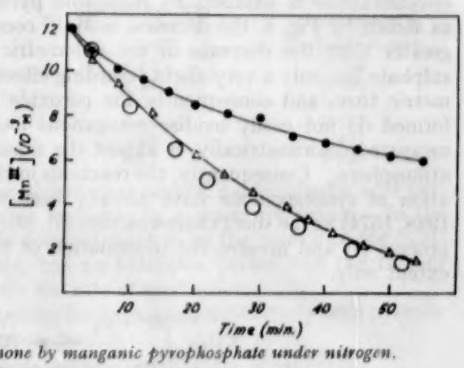


FIG. 3. *The prolonged oxidation of* cyclo*hexanone by manganic pyrophosphate under nitrogen.*

Temp. 50·0°; [Pyrophosphate], 0·169M; Initial [*cyclo*Hexanone], 1·52 × 10^{-2}M.
Upper curve, pH 0·42. Lower curve, pH 0·64.

FIG. 4. *The oxidation of* cyclo*hexanone by manganic pyrophosphate in the presence of oxygen.*

Temp. 25·0°; pH 0·38; [Pyrophosphate], 0·102M; initial concn. of *cyclo*hexanone, 4·85 × 10^{-2}M.
—△— Reaction in nitrogen; —●— reaction in oxygen (iodometry); —○— reaction in oxygen (Colorimetry).

of one and not two equivalents of Mn^{III}, it must be concluded that the mesomeric radical (I) very rapidly disproportionates, as indicated,* giving the cation (II) and anion (III) which, by immediate reaction with water are converted into 2-hydroxy*cyclo*hexanone (IV) and *cyclo*hexanone respectively. Some dimerisation of the radical (I) may, however, also occur.

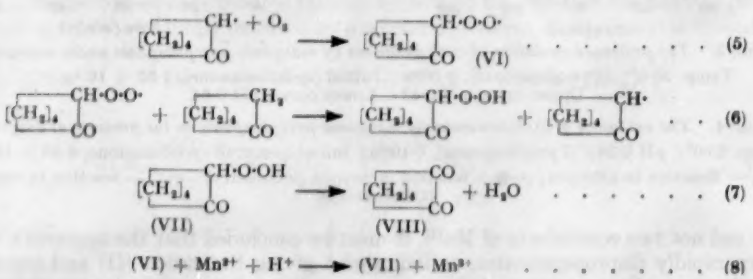
* Since (i) C–H bonds are much weaker than the H–O bonds of water, and (ii) there is no indication of the presence of either hydrogen atoms or hydroxyl radicals in the oxidising mixtures, we consider that disproportionation of the mesomeric radical (I) occurs by single-electron transfer, as indicated rather than by radical–water reactions, *e.g.*, $R\cdot + H_2O \longrightarrow RH + \cdot OH$; $R\cdot + \cdot OH \longrightarrow ROH$ or the converse, $R\cdot + H_2O \longrightarrow ROH + \cdot H$; $R\cdot + \cdot H \longrightarrow RH$. In addition, there is available from other studies of the reactions of free radicals much experimental evidence to indicate that free carbon radicals, $R_3C\cdot$, do not react with liquid water.

Route (4) for the oxidation has been supported by our isolation from oxidised solutions of 2-hydroxy*cyclo*hexanone (IV), which is attacked by manganic pyrophosphate about 10 times more slowly than is *cyclo*hexanone itself (see Table 8). The subsequent oxidation of the acyloin (IV) eventually leads, *via cyclo*hexane-1 : 2-dione, which has also been detected in oxidised solutions, to very extensive degradation: as many as 14·8 equivs. of Mn^{III} could be consumed per molecule of *cyclo*hexanone and some carbon dioxide is evolved. Fig. 3, however, shows that the rate of oxidation of *cyclo*hexanone becomes slower when about 2 equivs. of Mn^{III} have been consumed, as would be the case if the main reaction proceeded *via* the slowly oxidised 2-hydroxy*cyclo*hexanone. If dimerisation of radical (I) occurred in preference to disproportionation, then the decrease in oxidation rate would have been more marked when only one equiv. of Mn^{III} had been reduced.

Since ketones appear to be oxidised only after enolisation, and monohydric alcohols are not attacked by manganic pyrophosphate, the slowness of oxidation of 2-hydroxy-*cyclo*hexanone may perhaps be due to the diminution of its ketonic character by hydrogen-bonding as in structure (V).

The oxidation of diethyl ketone, under nitrogen, very closely resembles that of *cyclo*-hexanone. It is not retarded by adding several equivalents of vinyl cyanide, though polymerisation then occurs, is of first order with respect to the ketone (Table 6) and, at high concentrations of the oxidiser, eventually tends to approach zero order with respect to $[Mn^{III}]$ (Fig. 2, curve *B*). As many as 10—11 equivs. of manganic salt may be consumed per mole of ketone and, as carbon dioxide is liberated, the oxidation does not convert the diethyl ketone only into acetic acid.

(2) *Kinetic studies in the presence of oxygen.* A peroxide is undoubtedly formed when *cyclo*hexanone is oxidised by manganic pyrophosphate in the presence of oxygen, for, as shown by Fig. 4, the decrease in Mn^{III} concentration, measured colorimetrically, is far greater than the decrease in the iodometric titre. The initial addition of manganous sulphate has only a very slight retarding effect on both the change in $[Mn^{III}]$ and the iodometric titre, and consequently the peroxide radicals (VI) or molecules (VII) which are formed do not easily oxidise manganous ions. Again, the rate of decrease of $[Mn^{III}]$, measured colorimetrically, is almost the same in the presence of oxygen as in a nitrogen atmosphere. Consequently, the reactions in the presence of oxygen, which for the autoxidation of *cyclo*hexanone have already been represented by Robertson and Waters (*J.*, 1948, 1574) as the short chain-reaction (5), (6), and (7), compete with the disproportionation process (4) and involve the re-oxidation of manganous ions (reaction 8) to a very slight extent only.



Oxygen uptake rates have been measured by the Warburg technique, the solutions used being identical in composition and temperature with those employed for obtaining the data given in Fig. 4, and it was found that when all the manganic salt had been reduced 0·82 mole of oxygen had been absorbed per equiv. of Mn^{III} taken. Table 7 shows that 3—4 times as much oxygen is absorbed as can be accounted for as titratable peroxide, and consequently the breakdown of (VII) by reactions such as (7) must be fairly rapid. Further support for the occurrence of reactions (5), (6), and (7) in the presence of oxygen is given by the fact that much more *cyclo*hexane-1 : 2-dione (VIII) can be isolated, in the

form of the nickel complex of its dioxime, from oxidations under oxygen than from corresponding oxidations under nitrogen.

Corresponding measurements of the oxidation of diethyl ketone in presence of oxygen gave data of poor reproducibility : the oxygen greatly retards the destruction of Mn^{III} but the corresponding peroxide, if formed, seems to be very unstable.

Oxidations of Other Ketones.—With *cyclo*hexanone a limiting rate of oxidation can easily be reached at which the rate of destruction of Mn^{III} measured in equivalents equals the rate of enolisation of the ketone measured in moles, whilst with diethyl ketone it appears that a corresponding limiting oxidation rate could be reached at a much higher initial concentration of Mn^{III}. Table 2 compares oxidation rates and enolisation rates for a series of ketones in solutions of identical molarity and acidity. It will be seen that (*a*) the oxidation rate is always below the enolisation rate and (*b*) the two cyclic ketones differ from their analogues in having much higher reaction rates. The variation of the ratio (Oxidation rate)/(Enolisation rate) shows that the susceptibility of an enol towards one-electron abstraction cannot be related simply to the polar influences that are concerned in favouring or retarding, acid-catalysed enolisation of the corresponding ketone molecule. For instance, the enolic form of di*iso*propyl ketone is oxidised much more slowly than the enolic form of acetone, and in this respect our results do not accord with the conclusions of Shorter (*J.*, 1950, 3425) who invoked hyperconjugation to explain relative oxidation rates of ketones with ceric salts.

TABLE 2. *Oxidations of ketones with manganic pyrophosphate (under nitrogen).*

Temp. 40·0°; pH, 1·33; [Pyrophosphate], 0·128M.

Initial concns. (M × 10^{-3}) : [Mn^{III}], 1·47; [I_2], 1·87; [Ketone], 1·03.

Ketone	Oxidation rate [Equiv. (Mn^{III}) $l.^{-1}$ $hr.^{-1}$] × 10^{-3}	Enolisation rate (Mol. $l.^{-1}$ $hr.^{-1}$) × 10^{-3}	Oxidation rate / Enolisation rate
Me·CO·Me	0·42	1·47	0·289
Me·CO·Et	0·50	1·37	0·365
Et·CO·Et	0·56	1·09	0·513
Pr^i·CO·Pr^i	0·022	0·16	0·137
*cyclo*Pentanone	1·35	2·95	0·457
*cyclo*Hexanone	5·89	6·32	0·935

In previous parts of this series it has been shown that several oxidations by acid permanganate require initial attack on the organic molecule by a manganic cation. In the permanganate oxidation of *cyclo*hexanone this does not seem to be the case since the oxidation, even in the presence of pyrophosphate, has no induction period and the rate of oxidation does not appear to be connected with the rate of enolisation.

Oxidation of Pyruvic Acid.—Manganic pyrophosphate reacts quantitatively with pyruvic acid, under nitrogen to give acetic acid and carbon dioxide :

$$Me{\cdot}CO{\cdot}CO_2H + 2Mn^{III} + H_2O \longrightarrow Me{\cdot}CO_2H + 2Mn^{II} + CO_2 + 2H^+$$

Consequently, the corresponding enol, $CH_2{:}C(OH){\cdot}CO_2H$, which by analogy with the enolic forms of simple ketones should be more extensively oxidised, does not appear to be concerned. In this respect oxidation of pyruvic acid by manganic salt seems to be similar to that by potassium permanganate (Hatcher and Hill, *Trans. Roy. Soc. Canada*, 1928, [3], **22**, iii, 211), hydrogen peroxide (*idem*, *ibid.*), and ceric sulphate (Fromageot, *loc. cit.*). Indeed, it has been shown that the ceric sulphate oxidation of the enolic form of pyruvic acid proceeds more slowly than that of the ketonic form and that more than 2 equivs. of oxidant are consumed.

Pyruvic acid is so easily oxidised by manganic pyrophosphate that accurate kinetic measurements could be obtained only by lowering the reaction temperature to 10°. The reaction has the peculiar feature of being specifically retarded to a limited extent by manganous salt : as Tables 3 and 4 show, the oxidation reaches, at a certain Mn^{III} concentration, a steady lower value, after which a further five-fold increase in Mn^{II} concentration has no added effect. The extent of the percentage decrease in rate depends on the pH of the oxidising system but not on the concentration of the pyruvic acid. Zinc and magnesium ions have no corresponding action.

TABLE 3. *Effect of manganous sulphate on the oxidation of pyruvic acid.*

Temp. 10°; pH, 1·60; [Pyrophosphate], 0·504M.

Initial concentrations: $[Mn^{III}]$, $2{\cdot}08 \times 10^{-3}$M; [Me·CO·$CO_2H$], $7{\cdot}42 \times 10^{-3}$M.

Initial $[Mn^{II}]$ (10^{-3}M)	0·00	1·03	2·07	3·10	4·13	8·27	16·53
k_{unit} ($hr.^{-1}$)	0·216	0·211	0·205	0·202	0·199	0·200	0·198

TABLE 4. *Maximum extent of the retardation by manganous salts* (15°).

[Pyrophosphate], 0·404M; Initial $[Mn^{III}]$, $1{\cdot}77 \times 10^{-2}$M.

[Me·CO·CO_2H] (M × 10^{-2})	4·17	9·74	6·96	6·96	6·96	6·96
pH	2·26	2·26	2·26	1·37	1·23	1·05
% Decrease to limit	17·7	17·5	17·0	12·0	8·4	2·7

When pyruvic acid is present in excess the reaction is strictly of first order with respect to $[Mn^{III}]$ for 70—80% of the oxidation, provided that enough manganous salt has been added. The order with respect to pyruvic acid varies as [Pyruvic acid]/(a + [Pyruvic acid]) (see Table 9), and that with respect to pyrophosphate as 1/([Pyrophosphate] + b) (see Table 10), where in each case the concentrations of [Pyruvic acid] and [Pyrophosphate] correspond to the amounts of uncomplexed materials in solution (compare Part III), it being assumed that each Mn^{3+} ion forms complexes with three pyrophosphate groups and each Mn^{2+} ion with two.

These observations, apart from the curious effect of manganous ions, for which we can suggest no rational explanation, satisfactorily accord with the reaction mechanism below:

$$\{Mn(H_2P_2O_7)_3\}^{3-} + Me{\cdot}CO{\cdot}CO_2H \underset{\text{(Fast equilibrium)}}{\overset{K_1}{\rightleftharpoons}} \{Mn(H_2P_2O_7)_2,Me{\cdot}CO{\cdot}CO_2\}^{3-} + (H_2P_2O_7)^{2-} + H^+ \quad (9)$$

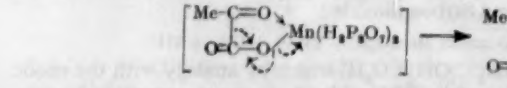
$$\{Mn(H_2P_2O_7)_2,Me{\cdot}CO{\cdot}CO_2\}^{3-} \xrightarrow[\text{(Slow)}]{k_2} \{Mn(H_2P_2O_7)_3\}^{3-} + Me{\cdot}CO\cdot + CO_2 \quad . \quad . \quad (10)$$

$$Me{\cdot}CO\cdot + Mn^{III} \longrightarrow (Me{\cdot}CO)^+ + Mn^{II} \text{ (Fast)} \quad . \quad . \quad . \quad . \quad . \quad (11)$$

$$(Me{\cdot}CO^+) + H_2O \longrightarrow Me{\cdot}CO_2H + H^+ \text{ (Fast)} \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

whence $$\frac{-\,d[Mn^{III}]}{dt} = \frac{2k_2K_1[Me{\cdot}CO{\cdot}CO_2H][Mn^{III}]}{[(H_2P_2O_7)^{2-}] + K_1[Me{\cdot}CO{\cdot}CO_2H]}$$

We favour the view that carbon dioxide is liberated in the primary oxidation process (10) because this accords with the following scheme for the rate-controlling breakdown of the manganic pyrophosphate–pyruvic acid complex in which chelation of the α-carbonyl group is important (compare the oxidation of pinacol, Part III).



This electron-switch cannot be reversible, for were that the case then there should be no limit to the retarding action of manganous ions (compare the oxidation of malonic acid, Part IV). Free radicals are undoubtedly formed, for if vinyl cyanide is added to the oxidising mixture insoluble polymer containing carbonyl groups separates. This addition of monomer slightly decreases the rate of reduction of Mn^{III}. Ethyl and *iso*propyl alcohol, both of which are oxidised by the malonic acid radical, neither affect the rate of the reaction nor are oxidised by the oxidising pyruvic acid, and consequently the free radical involved, which we tentatively suggest to be free acetyl, Me·CO·, has not a very high $E_{(+e)}$ value.

The variation of the oxidation velocity with acidity is shown in Fig. 5 (curve A). The decrease of the rate of oxidation with decreasing acidity in the pH ranges 0·5—0·8 and 2—3 can be expected from the known change of the redox potential of manganic pyrophosphate with pH (Watters and Kolthoff, *J. Amer. Chem. Soc.*, 1948, **70**, 2455; compare Part III) but the change at intermediate acidities cannot have this origin alone. Pyruvic is an unusually strong organic acid ($K_a = 3{\cdot}2 \times 10^{-3}$ at 25°) and consequently in the pH

range 0·8—1·8, in which the oxidation rate is increasing to a shallow maximum, the extent of the ionisation of the pyruvic acid is also increasing (Fig. 5, curve *B*). As the pH of the system is increased, equilibria of type (9) involving the pyruvate anion rather than the undissociated acid become increasingly important in providing the complex which is then degraded (reaction 10). It is to be expected that the equilibrium constant for the reaction of type (9) involving the pyruvate anion would be much greater than that involving the free acid, since the anion would much more readily form the manganic complex. The trend of curve *B* of Fig. 5 follows that of curve *A* in such a way as to support this view.

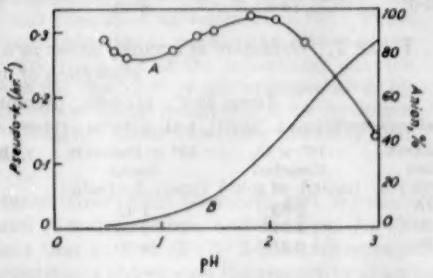


FIG. 5. *Curve A: The variation with* pH *of the rate of oxidation of pyruvic acid. Curve B: The extent of ionisation of pyruvic acid.*

Temp. 10·0°; [Pyrophosphate], 0·350M; initial concns. (M × 10^{-2}): [Mn^{III}], 1·87; [Mn^{II}], 1·16; [$Me{\cdot}CO{\cdot}CO_2H$], 6·95.

EXPERIMENTAL

Materials.—Sodium manganic pyrophosphate solutions were prepared as described in Part II (*loc. cit.*). After preliminary purification (*cyclo*pentanone and *cyclo*hexanone *via* bisulphite compounds; acetone *via* the sodium iodide compound) each ketone was shaken with ferrous sulphate, dried, and fractionally distilled under nitrogen. 2-Hydroxy*cyclo*hexanone was prepared by the method of Kötz *et al.* (*Annalen*, 1913, **400**, 55; *Org. Synth.*, 1945, **25**, 22); pyruvic acid was fractionated 3 or 5 times under nitrogen (b. p. 63—64°/10 mm.).

Kinetic Measurements.—Colorimetric analyses, rates of oxidation, and oxygen uptake rates were performed as described in Part IV (*loc. cit.*). Rates of enolisation were determined by adding solutions of the ketones to iodine–potassium iodide solutions buffered by pyrophosphate: aliquot parts were removed at intervals, quenched in saturated sodium acetate solution, and titrated with standard sodium thiosulphate.

Products of the Oxidation of cyclo*Hexanone.*—(a) *In the absence of oxygen.* After reaction the solution (2·5 l.; initial concns.: [Mn^{III}], 5·6 × 10^{-2} M; [*cyclo*hexanone], 2 × 10^{-2} M) was extracted continuously with ether for 8 hr. The dried extract on fractionation gave: (i) b. p. 55—63°/15—18 mm., colourless liquid (0·7 g.); (ii) b. p. 64—68°/15—18 mm., colourless liquid (2·5 g.); (iii) b. p. 70—100°/15—18 mm., pink solid (1·1 g.); (iv) residual gum (2·5 g.). Fractions (i) and (ii) were largely *cyclo*hexanone, but a portion of (ii) after conversion into the oxime gave a faint red precipitate when tested with nickel nitrate solution. The solid (iii) was crystallised (with very poor recovery) from ethanol; the white product did not depress the m. p. (135—137°) of 2-hydroxy*cyclo*hexanone.

(b) *In the presence of oxygen.* After reaction the solution (230 ml.; initial concns.: [Mn^{III}], 2·1 × 10^{-2}M, [*cyclo*hexanone], 1·4 × 10^{-2}M) was extracted with ether (5 × 150 ml.). After concentration to 10 ml. the ketonic residue was converted into the oxime by Rauh's method (*J. Org. Chem.*, 1945, **10**, 199); the crude product gave a red flocculent precipitate when added to neutral nickel nitrate solution.

TABLE 5. *Oxidation of* cyclo*hexanone under nitrogen: reaction order with respect to* cyclo*hexanone.*

Temp. 25·0°; pH 1·53; [Pyrophosphate], 0·153M; Initial [Mn^{III}], 1·84 × 10^{-2}M.

10^3 × Initial $[C_6H_{10}O]$ (M)	10^4 × Initial rate [equiv. (Mn^{III}) $l.^{-1}$ $hr.^{-1}$]	10^3 × Initial rate / Initial $[C_6H_{10}O]$	10^3 × Initial $[C_6H_{10}O]$ (M)	10^4 × Initial rate [equiv. $[Mn^{III}]$ $l.^{-1}$ $hr.^{-1}$]	10^3 × Initial rate / Initial $[C_6H_{10}O]$
9·81	10·0	10·2	34·3	33·2	9·68
14·7	14·3	9·73	39·3	37·5	9·57
19·6	19·4	9·89	44·2	43·2	9·77
30·1	28·4	9·43	49·1	47·1	9·59

TABLE 6. *Oxidation of diethyl ketone under nitrogen: reaction order with respect to diethyl ketone.*

Temp. 40·0°; pH 1·54; [Pyrophosphate], 0·153M; Initial [Mn^{III}], 1·85 × 10^{-3}M.

10^3 × Initial [$COEt_2$] (M)	10^4 × Initial rate [equiv. (Mn^{III}) $l.^{-1}$ $hr.^{-1}$]	100 × Initial rate / Initial [$COEt_2$]	10^3 × Initial [$COEt_2$] (M)	10^4 × Initial rate [equiv. (Mn^{III}) $l.^{-1}$ $hr.^{-1}$]	100 × Initial rate / Initial [$COEt_2$]
12·2	5·35	4·38	42·7	18·2	4·26
17·5	7·13	4·07	52·4	21·4	4·08
22·7	9·55	4·21	61·2	25·0	4·08
28·0	11·3	4·04	69·9	29·4	4·21
35·0	14·9	4·26	78·7	31·7	4·02

TABLE 7. *Oxidation of* cyclo*hexanone in oxygen: formation of peroxides and absorption of oxygen.*

Temp. 25·0°; pH 0·38; [Pyrophosphate], 0·102M.

Initial concentrations: [Mn^{III}], 1·21 × 10^{-3}M; [Mn^{II}], 2·41 × 10^{-3}M; [*cyclo*Hexanone], 4·85 × 10^{-2}M.

Reaction time (min.)	10^3 × O_2 absorbed (mole/l. of soln.)	10^3 × Peroxide found (equiv./l. of soln.)	Reaction time (min.)	10^3 × O_2 absorbed (mole/l. of soln.)	10^3 × Peroxide found (equiv./l. of soln.)
10	2·63	1·45	40	7·36	4·55
20	4·64	2·96	50	8·17	4·89
30	6·21	4·00			

TABLE 8. *Comparative oxidations of* cyclo*hexanone and of 2-hydroxy*cyclo*hexanone under nitrogen.*

[Pyrophosphate], 0·153M; Initial [Mn^{III}], 1·79 × 10^{-3}M; [Ketone], 4·44 × 10^{-2}M.

Temp.	pH	Initial rates of oxidation [equiv. (Mn^{III}) $l.^{-1}$ $hr.^{-1}$] *cyclo*Hexanone	2-Hydroxy*cyclo*hexanone
30·0°	0·49	2·88 × 10^{-3}	3·12 × 10^{-4}
40·0	1·10	2·76 × 10^{-3}	2·76 × 10^{-4}
40·0	1·10	Enolisation rate	4·18 × 10^{-4} (mole $l.^{-1}$ $hr.^{-1}$)

TABLE 9. *Oxidation of pyruvic acid under nitrogen: variation of rate with concentration of pyruvic acid.*

Temp., 10·0°; pH, 1·30; [Pyrophosphate], 0·435M.

Initial concentrations: [Mn^{III}], 1·79 × 10^{-3}M; [Mn^{II}], 1·08 × 10^{-3}M.

1/[Initl. concn. of *free* $C_3H_4O_3$] (l./mole)	1/[Pseudo-first-order const.] (hr.) Obs.	Calc.*	1/[Initl. concn. of *free* $C_3H_4O_3$ (l./mole)	1/[Pseudo-first-order const.] (hr.) Obs.	Calc.*
2·58	1·12	1·13	8·62	3·31	3·21
3·23	1·36	1·37	12·9	4·73	4·68
4·31	1·75	1·75	16·3	5·75	5·75
6·45	2·55	2·59	19·6	6·85	6·83

* From $1/k_1 = 0·306 + 0·333/[Me·CO·CO_2H]$.

TABLE 10. *Oxidation of pyruvic acid under nitrogen: variation of rate with concentration of pyrophosphate.*

Temp. 10·0°; pH 1·52; Initial concentrations (M × 10^{-2}): [Mn^{III}], 1·10; [Mn^{II}], 0·437; [$Me·CO·CO_2H$], 3·92.

(The ionic strength was kept approx. constant by replacing acid and pyrophosphate by 1·90M-KCl.)

Concn. of *free* pyrophosphate (M)	1/[Pseudo-first-order const.] (hr.) Obs.	Calc.†	Concn. of *free* pyrophosphate (M)	1/[Pseudo-first-order const.] (hr.) Obs.	Calc.†
0·169	5·62	5·65	0·341	9·26	9·34
0·193	6·29	6·20	0·389	10·3	10·4
0·243	7·14	7·25	0·414	10·9	10·9
0·292	8·55	8·35			

† From $1/k_1 = 2·14 + 21·2$ [Pyrophosphate].

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THE DYSON PERRINS LABORATORY, OXFORD. [*Received, July 17th,* 1954.]

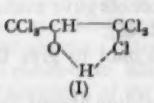
The Behaviour of 1 : 1 : 1 : 3 : 3 : 3-*Hexachloropropan-2-ol with Inorganic Non-metal Halides.*

By W. Gerrard and B. K. Howe.

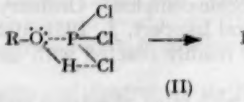
[Reprint Order No. 5630.]

The alcohol did not react with phosphorus trichloride, phosphorus oxychloride, thionyl chloride, silicon tetrachloride, or acetyl chloride, but reacted very slowly with phosphorus pentabromide, tribromide, or oxybromide. In the presence of pyridine, there was formation of esters at −10°. These results appear to be due to a drastic reduction in nucleophilic power of the hydroxyl-oxygen atom by the inductive effect of the substituent chlorine atoms, together with a reduction in the reactivity of the hydrogen atom by internal hydrogen bonding, both effects being compensated by hydrogen bonding with the base, ROH · · · NC_5H_5. Other reactions, including that with boron trichloride, are described.

Certain properties of trichloro-*tert.*-butanol (chloretone) (Gerrard, and Wyvill, *Research*, 1949, **2**, 536) and 2 : 2 : 2-trichloroethanol (Gerrard, Green, and Phillips, *J.*, 1954, 1148) have been described, and it is now evident that 1 : 1 : 1 : 3 : 3 : 3-hexachloropropan-2-ol is an example of the extreme influence of substituent chlorine on the reactivity of an alcoholic hydroxy-group. Under the conditions described the alcohol did not react with phosphorus trichloride, phosphorus oxychloride, thionyl chloride, silicon tetrachloride, or acetyl chloride; but it did so slowly with phosphorus pentabromide, tribromide, or oxybromide in boiling *n*-hexane. This could be due to the drastic reduction of electron availability on the oxygen atom caused by the accumulation of the inductive effect of each of six chlorine atoms, and to the reduction in availability of hydroxyl-hydrogen by internal hydrogen bonding (cf. I). Steric hindrance does not appear as the cause of this low reactivity, for the alcohol reacted readily with the reagents when pyridine was present.



(I)



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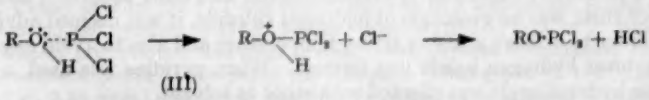
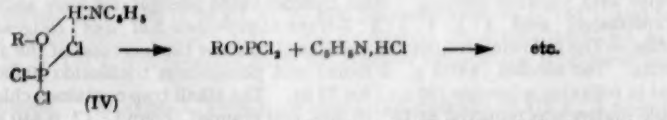


(III)

Taking phosphorus trichloride as an example, we adopt the view that the driving force of its primary interaction with an " ordinary " alcohol such as butan-1-ol is the nucleophilic attack of hydroxylic oxygen on phosphorus; but whether the hydroxyl-hydrogen atom is simultaneously removed by a four-centre mechanism (cf. II) involving only one transition state (cf. Gerrard, *J.*, 1939, 99; 1940, 218) or is removed by a subsequent step (III) has not yet been decided.



(IV)

In the presence of pyridine, the alcohol immediately afforded the trialkyl phosphite and base hydrochloride, and thus showed a remarkable increase in reactivity attributable to co-ordination (cf. IV), which could increase the electron availability on oxygen and break the internal hydrogen bonding. Cleverdon and Smith's dipole-moment work (*Chem. and Ind.*, 1948, 29) supports the view, previously put forward by Gerrard (*J.*, 1939, 99; 1940, 1940, 218), in favour of hydrogen bonding between pyridine and alcohol (R·OH·NC_5H_5).

It is clear that pyridine does not merely react with hydrogen chloride as it is formed, but must take part in removing the hydrogen and the chlorine from the reacting entities.

In the presence of pyridine, thionyl chloride immediately afforded the dialkyl sulphite, but, in marked contrast with the sulphites of ordinary alcohols (cf. Gerrard, *J.*, 1939, 99; 1940, 218; French and Gerrard, *J.*, 1949, 3326), this did not react with thionyl chloride in the presence of pyridine hydrochloride even at 140°. Therefore Darzens's procedure (*Compt. rend.*, 1911, **152**, 1314, 1601) does not give the alkyl chloride.

In the presence of base, silicon tetrachloride readily reacted with the alcohol to the extent of three atoms of chlorine to give an alkoxysilane; but there was difficulty over the fourth. Similar replacement of chlorine in phosphorus oxychloride by alkoxyl in the presence of pyridine was virtually restricted to two chlorine atoms, and even the replacement of the second was very slow. However, when the oxybromide was used, two atoms of bromine were much more readily replaced, but under the conditions employed no further reaction took place. The phosphorobromidate, $POBr(OR)_2$, was obtained as white crystals, and was somewhat resistant to hydrolysis.

The phosphite showed reluctance to be dealkylated by hydrogen chloride and hydrogen bromide. On prolonged heating with hydrogen bromide, the phosphite afforded the alcohol, probably owing to attachment of bromine to phosphorus and of hydrogen to oxygen: $P(OR)_3 + HBr \longrightarrow PBr(OR)_2 + ROH$, etc. The basic function of the lone pair of electrons on the phosphorus atom appears to have been obliterated, and the phosphorus atom has become reluctantly electrophilic. The phosphites of ordinary alcohols quickly give alkyl bromide by a mechanism which is most probably represented by

$$P(OR)_3 + HBr \longrightarrow Br^- + PH^+(OR)_3 \longrightarrow RBr + O{:}PH(OR)_2$$

(Gerrard, *J.*, 1945, 848; Gerrard and Whitbread, *J.*, 1952, 914). This phosphite, like that of 2 : 2 : 2-trichloroethanol (Gerrard *et al.*, *J.*, 1954, 1148), gave the trialkyl phosphate, and not the chloridate, with chlorine. A similar result was obtained with bromine.

The reaction between the alcohol and boron trichloride alone slowly afforded trialkyl borate, but was not rapid enough in the presence of pyridine to compete successfully with the quick formation of pyridine–boron trichloride complex. Ordinary alcohols gave mainly the borate in these circumstances (Gerrard and Lappert, *J.*, 1951, 1020, 2545).

In the presence of base, acetyl chloride readily reacted with the alcohol to give the acetate in good yield.

Preliminary experiments were conducted with ether as solvent and pyridine absent and, since there was no evolution of hydrogen chloride, it was deemed advisable to use *n*-hexane in order to achieve a higher reflux temperature and also to avoid any retention by ether of whatever hydrogen halide was formed. When pyridine was used, a cleaner separation of base hydrochloride was effected with ether as solvent.

In hundreds of experiments on the interaction of alcohols and non-metallic inorganic halides in the presence of pyridine, no difference in reactivity has yet been detected according to whether the solvent was ether, *n*-pentane, or *n*-hexane.

Experimental

All solvents were vigorously dried, all reagents were purified, and liquids were mixed slowly dropwise with vigorous shaking. Base hydrochloride precipitates were analysed.

Experiments with 1 : 1 : 1 : 3 : 3 : 3-*Hexachloropropan-2-ol and Reagents in Absence of Pyridine.*—The following results are mentioned to show the inertness of the alcohol towards the reagents. The alcohol (4·002 g., 3 mols.) and phosphorus trichloride (0·687 g., 1 mol.) were heated in refluxing *n*-hexane (50 c.c.) for 72 hr. The alkali trap contained chloride ion (0·007 g.). Volatile matter was removed at 15°/20 mm. and trapped (Found: Cl, 0·440 g.), and the residue of alcohol (4·001 g.) had m. p. 87°, mixed m. p. 87°. Similarly the alcohol was quantitatively recovered when it (5·336 g., 2 mols.) was heated in *n*-hexane with thionyl chloride (1·190 g., 1 mol.) for 72 hr. Similarly the alcohol (5·336 g., 4 mols.), m. p. 88°, was recovered after being heated in *n*-hexane with silicon tetrachloride (0·850 g., 1 mol.) for 72 hr. The alcohol (2·668 g., 1 mol.) and acetyl chloride (0·785 g., 1 mol.) were heated in *n*-hexane (20 c.c.) for 72 hr., and the final residue (2·712 g.) gave purified alcohol (2·50 g.), m. p. 86°.

When phosphorus oxychloride (0·767 g., 1 mol.) and the alcohol (4·002 g., 3 mols.) were heated in *n*-hexane (35 c.c.) for 72 hr., no hydrogen chloride was evolved, and all the chlorine of the oxychloride remained easily hydrolysable. The oxybromide (0·717 g., 1 mol.) and alcohol (2·001 g., 3 mols.) under similar conditions afforded about one-sixth of the bromine as hydrogen bromide during 86 hr. Addition of pyridine and ethanol to the resulting solution gave base hydrobromide (Found: Br, 0·404 g.). Similarly the tribromide (0·677 g., 1 mol.) and alcohol (2·001 g., 3 mols.) gave hydrogen bromide (0·182 g.) during 72 hr., and the residue gave base hydrobromide (Found: Br, 0·379 g.). From the alcohol (4·002 g.) and tribromide (1·354 g.), all volatile matter including unchanged tribromide being removed *in vacuo*, the alcohol (1·85 g. after several recrystallisations from *n*-hexane), m. p. 88°, was recovered. The pentabromide (0·431 g., 1 mol.) and alcohol (1·334 g., 5 mols.) under similar conditions afforded hydrogen bromide (0·134 g.) during 86 hr., and the residue contained unchanged pentabromide (Found: Br, 0·276 g.).

Boron trichloride (1·445 g., 1 mol.) in *n*-hexane (100 c.c.) (at −10°) was added to a suspension of the alcohol (9·886 g., 3 mols.) in *n*-hexane (100 c.c.) at −80°. No reaction was apparent until after the mixture had remained at 0° for 2 hr. The mixture was kept at 10° for about 12 hr., whereupon the absorption tubes contained chlorine (0·0631 g.) and boron (0·0032 g.); it was then heated under reflux for 6 hr., and the fresh tubes then contained chlorine (0·9822 g.) and boron (0·0086 g.). The solvent was removed *in vacuo*, and the condensed liquid contained no ionisable chlorine. The residue of *trialkyl borate* (10·024 g. Calc.: 10·236 g.) had m. p. 322° (m. p. 312—313° after repeated recrystallisation from toluene in which it had limited solubility) (Found: C, 14·5; H, 0·9; Cl, 78·4; B, 1·35. $C_9H_3O_3Cl_{18}B$ requires C, 13·35; H, 0·35; Cl, 79·0; B, 1·34%). After being recrystallised from chloroform, the borate had m. p. 325° (Found: C, 14·6; H, 0·7; Cl, 78·9; B, 1·34%), but the m. p. returned to 313° on recrystallisation from toluene. Only 12% was hydrolysed by 0·1N-sodium hydroxide during 7 days, and even after the mixture was heated under reflux for 2 hr. the 7% hydrolysis was accompanied by removal of chlorine from alkyl group. The boron content was determined by heating the ester (*ca.* 1·5 g.) under reflux with methanol (40 c.c.) and concentrated sulphuric acid (2 c.c.) for 2 hr. and then distilling off the trimethyl borate for hydrolysis and titration in the usual way.

A toluene solution (150 c.c.) of the alcohol (16·008 g., 6 mols.) and boric acid (0·618 g., 1 mol.) was heated under reflux for 5 hr., water being removed by anhydrous copper sulphate in a Soxhlet thimble (cf. Dupire, *Compt. rend.*, 1936, **202**, 2086). More boric acid (0·618 g.) was added, and heating was continued overnight. The borate (6·16 g., 38%) separated from the cooled solvent. After recrystallisation from toluene it had m. p. 310°, and after recrystallisation from chloroform, 324·5°.

Interaction of the Alcohol and Reagents in the Presence of Pyridine.—Phosphorus trichloride. The trichloride (1·375 g., 1 mol.) in ether (10 c.c.) was added dropwise to a well-shaken mixture of the alcohol (8·004 g., 3 mols.) and pyridine (2·373 g., 3 mols.) in ether (20 c.c.) at −10°. Base hydrochloride was immediately precipitated, and after several hours at room temperature the mixture was filtered. The residue (5·236 g.) comprised the phosphite (1·808 g.), m. p. 156°, and base hydrochloride (2·947 g., 2·55 mols.) which was removed by water. The ethereal solution afforded crude phosphite (6·3 g.), m. p. 150°, and after recrystallisation from ethyl acetate the yield of *tris*-1 : 1 : 1 : 3 : 3 : 3-*hexachloroisopropyl phosphite*, m. p. 161°, as white rhombic crystals, was 6·71 g. (81%) (Found: C, 13·35; H, 0·15; Cl, 78·0. $C_9H_3O_3Cl_{18}P$ requires C, 13·05; H, 0·35; Cl, 77·05%).

Phosphorus tribromide. Similarly the alcohol (24·012 g., 3 mols.), pyridine (7·122 g., 3 mols.), and the tribromide (8·123 g., 1 mol.) in ether (90 c.c.) at −20° gave an immediate precipitate of base hydrobromide. After 2 days at room temperature, the mixture was filtered. The residue (21·28 g.) comprised phosphite (8·35 g.), m. p. 158° (recrystallised, m. p. 161°), and base hydrobromide (14·26 g., 2·97 mols.) which was removed by water. Phosphite (16·55 g.), m. p. 158° (recrystallised, m. p. 161°), was obtained from the ethereal filtrate, the total yield being 21·97 g. (78·8%).

Phosphorus oxychloride. The alcohol (8·004 g., 3 mols.) and pyridine (2·373 g., 3 mols.) in ether (40 c.c.) were added to the oxychloride (1·534 g., 1 mol.) in ether (50 c.c.) at −10°. Precipitation of base hydrochloride was slow, and at the end of the mixing (1 hr.) about 1 mol. had separated. After 3 days at room temperature the mixture was filtered. The residue (2·342 g.) comprised alcohol (0·920 g.) and base hydrochloride (1·248 g., 1·08 mols.). This represents one of the three atoms of chlorine in the oxychloride. More salt (0·405 g., 0·35 mol.; mixed with alcohol, 0·210 g.) separated during 10 days. The solution was finally heated under reflux for 20 hr., whereafter from the cooled solution the salt (0·162 g., 0·14 mol.) and an

unidentified substance (0·108 g.), m. p. 140—150°, were precipitated. Removal of ether gave a residue (7·27 g.) of viscous heterogeneous material which has not yet been examined.

Phosphorus oxybromide. This reagent was prepared from phosphorus pentabromide and *iso*propanol as described by Gerrard, Nechvatal, and Wyvill (*Chem. and Ind.*, 1947, 437). Different orders of addition being tried, it was found that precipitation of base hydrobromide was fairly quick at −20°, but involved only two of the three bromine atoms. The mixture was allowed to remain at 15° for 3 days before filtration. The alcohol (8·004 g., 3 mols.) and pyridine (2·373 g., 3 mols.) in ether (40 c.c.) were added to the oxybromide (2·867 g., 1 mol.) in ether (40 c.c.) at −10°. The precipitate comprised base hydrobromide (3·296 g., 2·06 mols.) and a water-insoluble substance (0·592 g.), m. p. *ca.* 100°. Removal of ether at 15 mm. afforded a solid residue (9·17 g.), which was dissolved in hot *n*-heptane and a little ether, washed with water (2 × 40 c.c.), and dried. On removal of solvent, the residue which was insoluble in *n*-heptane had m. p. *ca.* 100°, and the *n*-heptane gave on concentration a solid at 0°, m. p. *ca.* 98°. Repeated recrystallisation of the latter by cooling its solution in boiling ethyl acetate and light petroleum (b. p. 100—120°) afforded a white solid, m. p. 282°, probably the pyrophosphate, $(RO)_2P(:O)\cdot O\cdot P(:O)(OR)_2$. When the primary ethereal filtrate was not washed with water, *bis*-1 : 1 : 1 : 3 : 3 : 3-*hexachloroisopropyl phosphorobromidate* (89% yield), m. p. 120° after recrystallisation from *n*-hexane (Found: C, 11·15; H, 0·4; Cl, 64·1; Br, 12·0; P, 4·2. $C_6H_2O_3Cl_{12}BrP$ requires C, 10·95; H, 0·3; Cl, 64·6; Br, 12·1; P, 4·7%), was obtained as white needles. Bromide ion was only slowly formed by hydrolysis with water; after being in contact with water and acetone for 4 hr. at room temperature, the bromidate was 10% hydrolysed, and the remainder, m. p. 120—121°, was quantitatively recovered. The bromidate reacted slowly with octanol in the presence of pyridine and ether at 15°. After 6 days what was probably the *mixed phosphate*, m. p. 194° after recrystallisation from *n*-hexane (Found: C, 20·1; H, 1·65; Cl, 61·5; P, 4·5. $C_{14}H_{19}O_4PCl_{12}$ requires C, 23·75; H, 2·7; Cl, 60·1; P, 4·4%), was obtained in 15% yield; and much of the bromidate, m. p. 119°, mixed m. p. 119°, was recovered.

Thionyl chloride. There was immediate precipitation of base hydrochloride (6·554 g., 1·89 mol.) when a solution of the alcohol (16·008 g., 2 mols.) and pyridine (4·746 g., 2 mols.) in ether (60 c.c.) was added to thionyl chloride (3·569 g., 1 mol.) in ether (100 c.c.) at −10°. Next morning, the solid was filtered off, and from the ethereal filtrate crude sulphite (quantitative), m. p. 58—62°, was obtained. On recrystallisation from light petroleum (b. p. 100—120°), a white solid, m. p. 64° was obtained, but the sulphite could not be completely freed from the alcohol, into which it appeared to decompose during a number of recrystallisations from *n*-hexane (Found: C, 12·9; H, 0·0; Cl, 74·0; S, 4·95. Calc. for $C_6H_3O_3Cl_{12}S$: C, 12·45; H, 0·35; Cl, 73·4; S, 5·5%).

Heptachloropropane could not be obtained from the sulphite by interaction with thionyl chloride in the presence of base hydrochloride (1 mol. or small amounts). The sulphite (17·20 g., 1 mol.) was mixed with thionyl chloride (3·57 g., 0·5 mol.) and base hydrochloride (0·08 g.). No reaction was apparent at 80° (1 hr.), nor at 100° (1 hr.); and at 140° (2 hr.) thionyl chloride distilled through the column. The distillate was returned, and the mixture kept at 15° overnight and, on being reheated, gave thionyl chloride (3·01 g.). The residue decomposed at 200°/10 mm., and afforded several distillates, from which heptachloropropane could not be isolated.

Silicon tetrachloride. With the tetrachloride (1·699 g., 1 mol.), pyridine (3·164 g., 4 mols.), and the alcohol (10·672 g., 4 mols.) in *n*-pentane (70 c.c.) at 20—25°, there was an immediate precipitation of base hydrochloride, which was estimated as 3·3 mols., whereas the alcohol (about 1·7 g.) was recovered. Little could be done with the thick oil (8·61 g.) left by the evaporated solvent. When the alcohol (8·004 g.) and pyridine (2·373 g.) were restricted to 3 mols. for 1 mol. of tetrachloride (1·699 g.) only 2·2 mols. of base hydrochloride were precipitated from ethereal solution. Again the sticky residue (7·89 g.) from the ether was intractable.

In attempts to obtain crystalline solids, octyloxychlorosilanes were used. These were prepared by the addition of octan-1-ol (65 g., 1 mol.) in ether (40 c.c.) to silicon tetrachloride (85 g., 1 mol.) in ether (25 c.c.) at 0°, nitrogen being passed into the mixture. After 1 hr., volatile matter was removed at 15°/15 mm., and after protracted fractionations the following liquids together with mixtures were obtained: octyloxytrichlorosilane (84·0 g.), b. p. 105°/9 mm., $n_D^{20\cdot5}$ 1·4315 (Found: Cl, 40·3. Calc. for $C_8H_{17}OCl_3Si$: Cl, 40·35%); dioctyloxydichlorosilane (21·4 g.), b. p. 138—140°/0·5 mm., $n_D^{20\cdot5}$ 1·4360 (Found: Cl, 19·95. Calc. for $C_{16}H_{34}O_2Cl_2Si$: Cl, 19·85%), and trioctyloxychlorosilane (9·1 g.), b. p. 175—180°/0·5 mm., $n_D^{20\cdot5}$ 1·4373 (Found: Cl, 9·7. Calc. for $C_{24}H_{51}O_3ClSi$: Cl, 8·15%).

The trichlorosilane (2·637 g., 1 mol.) in ether (20 c.c.) was added to the alcohol (8·004 g.,

3 mols.) and pyridine (2·373 g., 3 mols.) in ether (50 c.c.) at −20°. Base hydrochloride was immediately formed. Next morning the precipitate was filtered off, and it comprised hydrochloride (2·589 g., 2·24 mols.) and the alcohol (1·337 g.), m. p. 86°. The ethereal filtrate gave a viscous oil (9·03 g.). Similarly the dichlorosilane (3·574 g., 1 mol.), pyridine (1·582 g., 2 mols.), and the alcohol (5·336 g., 2 mols.) gave base hydrochloride (2·243 g., 1·94 mol.), unchanged alcohol (0·152 g.), and a residue (8·02 g.), which, after being redissolved in ether, washed, and dried, afforded a liquid, probably the mixed *di*-n-*octyloxydi*-1 : 1 : 1 : 3 : 3 : 3-*hexachloroisopropoxysilane* (Found : Cl, 52·1; Si, 3·5. $C_{22}H_{36}O_4Cl_{12}Si$ requires Cl, 51·9; Si, 3·45%).

Boron trichloride. The analysis of this system was protracted. The trichloride (1·058 g., 1 mol.) in *n*-hexane (20 c.c.) was added to the alcohol (7·224 g., 3 mols.) and pyridine (2·142 g., 3 mols.) in *n*-hexane (50 c.c.) at 20° (at lower temperatures the alcohol separates). Next morning the precipitate was filtered off, and the filtrate gave a viscous liquid (6·46 g.) which slowly solidified (several days). It afforded pyridine (0·77 g.) and the alcohol (5·45 g., 75·4% recovery), m. p. and mixed m. p. 87°. The precipitate (2·488 g.) comprised pyridine hydrochloride (0·705 g.) and a water-insoluble material (2·349 g.) which softened at 75°, melted with decomposition at 210°, and appeared to comprise pyridine–boron trichloride complex (1·119 g.) and some alkoxyboron chloride.

Reactions with the Phosphite.—At room temperature there was a period of 30 min. before chlorine reacted with the phosphite, and then a vigorous, exothermic reaction ensued. The dry gas was passed into a solution of the phosphite (2·073 g.) in ether at −10° for 1·5 hr.; but no absorption occurred. During the evaporation of the solvent *in vacuo* at room temperature (10 min.) the vigorous reaction again occurred, and a phosphine-like odour was detected. More ether was added, and complete saturation with gas at room temperature was effected. Volatile matter was removed *in vacuo*, and the white *tris*-1 : 1 : 1 : 3 : 3 : 3-*hexachloroisopropyl phosphate* (1·82 g.) had m. p. 182° unchanged on recrystallisation from *n*-hexane (Found : C, 13·05; H, 0·75; Cl, 75·5; P, 3·7. $C_9H_3O_4Cl_{18}P$ requires C, 12·8; H, 0·35; Cl, 75·6; P, 3·65%). By means of carbon dioxide bromine vapour was passed into the phosphite (2·156 g.) at room temperature. Removal of volatile matter *in vacuo* afforded a residue (2·12 g.), m. p. 182° unchanged on recrystallisation from *n*-hexane (Found : C, 13·05; H, 0·55; Cl, 73·85; P, 3·7%). The m. p. was undepressed by the previous specimen of phosphate. There was no easily hydrolysable halogen present.

The phosphite (4·145 g., 1 mol.) was recovered, m. p. and mixed m. p. 160°, after it had been heated with ethyl iodide (0·780 g., 1 mol.) in chloroform (10 c.c.) for 40 hr. at 100°.

Dry hydrogen chloride was passed into the phosphite (4·145 g.) in ether (10 c.c.) for 10 hr. at 20°. After removal of volatile matter, the residue (4·13 g.), m. p. 148°, was dissolved in hot *n*-hexane and treated with charcoal, and the solution was filtered and cooled. Phosphite (2·3 g., 55·5%), m. p. 160°, and, from the mother-liquor, more phosphite (1·2 g.) were obtained, the total recovery being 84·5%.

Dry hydrogen bromide was passed into the phosphite (3·481 g.) in ether (10 c.c.) for 3 hr. at 20°. Removal of volatile matter *in vacuo* gave a solid (3·285 g.), m. p. 142°, which, after repeated recrystallisation from *n*-hexane, gave the phosphite (0·61 g.), m. p. 158° (Found : C, 13·35; H, 0·15; Cl, 78·2. Calc. : C, 13·05; H, 0·35; Cl, 77·05%). A solution of the phosphite (6·004 g.) in ether (200 c.c.) was saturated with hydrogen bromide (6·5 hr.) and stored for 2 days. It was heated under reflux for 6 hr., and volatile matter was removed at 20°/20 mm. The red fuming liquid (7·38 g.) afforded the alcohol (3·95 g.), m. p. 87—88° (Found : C, 13·85; H, 0·85; Cl, 80·3. Calc. for $C_3H_2OCl_6$: C, 13·5; H, 0·75; Cl, 79·75%), which was extracted by hot *n*-hexane. The residue contained bromine.

The Alcohol, Acetyl Chloride, and Pyridine.—The alcohol (4·002 g., 1 mol.) and pyridine (1·187 g., 1 mol.) in ether (50 c.c.) were added to acetyl chloride (1·177 g., 1 mol.) in ether (100 mm.) at −15°. Base hydrochloride was formed at once, and the precipitate comprised alcohol (0·325 g.) and hydrochloride (1·711 g., 0·987 mol.). The filtrate residue (4·635 g.) had m. p. 42°, m. p. 45° after repeated recrystallisation from light petroleum (b. p. 100—120°), and was the *acetate* (white platelets) (Found : C, 19·65; H, 1·45; Cl, 68·5. $C_5H_4O_2Cl_6$ requires C, 19·45; H, 1·3; Cl, 68·9%).

Preparation of Hexachloroacetone.—Difficulty has been experienced in our attempts to prepare hexachloroacetone by procedures described in the literature. By passing chlorine into monochloroacetone at temperatures up to 100° (F.P. 816,956, *Chem. Zentr.*, 1938, I, 2216; F.P. 837,741, *Chem. Zentr.*, 1939, II, 228), little better than the tetrachloroacetone was obtained. Granacher, Usteri, and Geiger (*Helv. Chim. Acta*, 1949, **32**, 703) had a similar experience. Edwards, Evans, and Watson (*J.*, 1937, 1942) did not give quantities of reactants or yields

of product in describing their procedure; but Dr. H. B. Watson kindly gave us the necessary information. Chlorine was passed into a refluxing and stirred mixture of tetrachloroacetones (1425 g.) (prepared by chlorinating acetone), acetic acid (90%, 1·72 l.), and sodium acetate (71 g.) under ultra-violet light for 55 hr., and then without it for a further 54 hr. Water (5 l.) was added; the oil was dried (Na_2SO_4) and distilled (b. p. 80—110°/13 mm.). Extraction of the aqueous layer with chloroform (5 × 150 c.c.; and then continuously for 10 hr.), followed by low-pressure removal of solvent from the dried solution, afforded a distillate, b. p. 60—200°/13 mm., which was combined with the former distillate; the whole was fractionated through a 75 × 2·5 cm. column packed with single-turn glass helices, jacketed electrically, and fitted with a variable take-off, total reflux head. Hexachloroacetone (520 g., 35%), b. p. 110°/40 mm., n_D^{20} 1·5103 (Found: C, 13·55; Cl, 80·5. Calc. for C_3OCl_6: C, 13·6; Cl, 80·3%), and pentachloroacetone (16%) were obtained, and tetrachloroacetone (30%) was recovered.

Reduction of Hexachloroacetone (cf. Geiger, Usteri, and Granacher, *Helv. Chim. Acta*, 1951, **34**, 1335).—The ketone (26·5 g.) in ether (50 c.c.) was added (1 hr.) to a suspension of lithium aluminium hydride (1·2 g.) in ether (50 c.c.). Mixing being complete (−10°), the mixture was stirred for 2 hr. at 0° and then cautiously added to ice (200 g.) and 2N-sulphuric acid (100 c.c.). The ethereal layer was separated, the aqueous layer extracted several times with ether, and the combined solution, after being dried (Na_2SO_4), afforded 1 : 1 : 1 : 3 : 3 : 3-hexachloropropan-2-ol (95%), b. p. 124°/10 mm., needles, m. p. 87—88° (Found: C, 13·45; H, 0·75; Cl, 79·3. Calc. for $C_3H_2OCl_6$: C, 13·5; H, 0·75; Cl, 79·75%). When the reduction was carried out at 35°, the yield was 81%. Information about two patents by Woolf and Gilbert (U.S. 2,635,117—8/1953) concerning the preparation of polychloroacetones has recently become available.

Choice of Solvent.—So far as solubility is concerned, ether is a more convenient solvent than *n*-hexane; but as preliminary experiments with ether as solvent gave no sign of reaction, it was deemed desirable to use *n*-hexane in order to achieve a higher reflux temperature and at the same time considerably reduce any retention of hydrogen chloride which would be formed if reaction had occurred to any appreciable extent. The following result illustrates the behaviour when ether was used as solvent. Hexachloropropan-2-ol (4·002 g., 3 mol.) in dry ether (35 c.c.) was added to phosphorus trichloride (0·687 g., 1 mol.), and the mixture was heated under reflux for 72 hr. No hydrogen chloride was absorbed in the trap containing potassium hydroxide. Unchanged phosphorus trichloride was removed *in vacuo* with the ether and condensed in a liquid-nitrogen trap (Found: Cl, 0·507 g. Cl in system: 0·532 g.). The residue (4·008 g.) had m. p. 85—86°, alone or mixed with hexachloropropan-2-ol. Thus recovery of the alcohol was 100%.

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Cyclic Amidines. Part III. 2-Acylamino-4-alkoxyquinolines.*

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The preparation of a number of 2-acylamino-4-alkoxyquinolines is described. 2 : 4-Dihydroxy- and 2-amino-4-hydroxy-quinoline afford the 3-bromo-derivatives on bromination. None of the compounds possessed useful biological activity.

The ready availability of 2-amino-4-hydroxyquinoline (Part II *) prompted this investigation of the preparation of its ethers and acyl derivatives for biological study.

A considerable excess of diazomethane was required for the methylation of the hydroxyl group of 2-amino-4-hydroxyquinoline. Its silver or sodium salt with methyl iodide afforded only 5% of the desired product. However, homologous ethers were obtained in satisfactory yield by treatment of the silver salt with an alkyl halide or alkylene dihalide. Evidence for their being 4-alkoxyquinolines was provided by dealkylation. The product obtained by treatment of the silver salt with ethyl bromide afforded 2-amino-4-hydroxyquinoline on being boiled with aqueous hydrobromic acid; the corresponding *n*-butyl ether was

* Part II, *J.*, 1954, 3878.

converted as described below into 4-*n*-butoxy-2-hydroxyquinoline which furnished 2 : 4-dihydroxyquinoline when distilled with aqueous hydrobromic acid. An attempt to effect an alkoxyl interchange with 2-amino-4-butoxyquinoline in the manner described for other 4-alkoxyquinolines (Berinzaghi, Deulofeu, Labriola, and Muruzabal, *J. Amer. Chem. Soc.*, 1943, **65**, 1357) was unsuccessful.

2-Amino-4-methoxyquinoline was acylated in boiling benzene in the presence of triethylamine. The formation of 2-acetamido-4-methoxyquinoline both by acetylation and methylation served to confirm the constitution assigned to the product of acetylation of 2-amino-4-hydroxyquinoline.

2-Amino-4 : 8-dihydroxyquinoline, its 5-methyl homologue, and 2-amino-4 : 6-dihydroxyquinoline were obtained by demethylation of the corresponding 2-amino-4-hydroxy-6- or -8-methoxyquinolines. Interaction of ethyl cyanoacetate and *o*-hydroxyanilinium benzenesulphonate did not furnish 2-amino-4 : 8-dihydroxyquinoline; the products obtained were 2-methylbenzoxazole, *oo'*-dihydroxymalondianilide, and ammonium benzenesulphonate. The production of benzoxazoles from salts of *o*-hydroxyaniline and nitriles has been described by Hölljes and Wagner (*J. Org. Chem.*, 1944, **9**, 31) and we have observed the loss of the ethoxycarbonyl group in reactions of the foregoing type (Part II, *loc. cit.*).

On treatment with nitrous acid in solution in concentrated sulphuric acid, 2-amino-4-*n*-butoxyquinoline afforded 4-*n*-butoxy-2-hydroxyquinoline; in hydrochloric acid, the product contained also 4-*n*-butoxy-2-chloroquinoline.

Bromination of 2-amino-4-hydroxyquinoline in glacial acetic acid furnished a monobromo-derivative which on treatment with nitrous acid gave the same bromo-2 : 4-dihydroxyquinoline, m. p. 232—233° (decomp.), as was obtained by a similar bromination of 2 : 4-dihydroxyquinoline. The same monobromo-derivative, together with a dibromo-derivative, was formed when the bromination was carried out in formic acid (98—100%). It appeared likely that monobromination would occur in the 3-position in both cases. If the 3-position were free in the 2-amino-bromo-4-hydroxyquinoline, interaction with nitrous acid would, by analogy with the behaviour of 2-amino-4-hydroxyquinoline (Gabriel, *Ber.*, 1918, **51**, 1500) and 2 : 4-dihydroxyquinoline (Baeyer and Homolka, *Ber.*, 1883, **16**, 2216), afford a 3 : 4-dihydro-3-hydroxyiminoquinoline. Further, nitration of 2 : 4-dihydroxyquinoline (Gabriel, *loc. cit.*), and bromination of 4-hydroxyquinoline (Riegel, Lappin, Albisetti, Adelson, Dodson, Ginger, and Baker, *J. Amer. Chem. Soc.*, 1946, **68**, 1229; Schofield and Swan, *J.*, 1950, 384) and 2-hydroxylepidine (Knorr, *Annalen*, 1886, **236**, 69), result in the entry of the substituent in the 3-position. Meyer and Heimann (*Compt. rend.*, 1936, **203**, 264) state that 3-bromo-2 : 4-dihydroxyquinoline, prepared by bromination of 2 : 4-dihydroxyquinoline in formic acid (100%), has m. p. 281° and that its orientation can be proved by oxidation with potassium permanganate to 3-bromo-2 : 4-dihydroxyquinolinic acid; no confirmatory analytical data are provided. We find that the behaviour of 2 : 4-dihydroxyquinoline on oxidation with potassium permanganate is similar to that of 4-hydroxyquinoline (Friedländer and Ostermaier, *Ber.*, 1882, **15**, 332); isatin is produced in both cases. The bromo-2 : 4-dihydroxyquinoline, m. p. 232—233° (decomp.), prepared by us, similarly afforded isatin. Accordingly, we believe the bromine to occupy the 3-position in this bromo-2 : 4-dihydroxyquinoline and hence also in the 2-amino-bromo-4-hydroxyquinoline.

Many of the compounds described in this communication were weakly spasmolytic when tested against acetylcholine and histamine but the effect was much less than that of known antagonists; the most active was 2-benzamido-4-methoxyquinoline. Some amœbicidal activity was exhibited *in vitro* by 2-amino-4-propoxyquinoline and its homologues but was not retained *in vivo*.

Experimental

2-Amino-4-methoxyquinoline.—A solution of 2-amino-4-hydroxyquinoline (16 g.) in methanol (400 c.c.) was treated at 3° with nine successive quantities of a wet ethereal solution (130 ml.) of diazomethane each prepared from nitrosomethylurea (14 g., 120 mols.) during 6 hr. After 3 days, the solvent was evaporated under reduced pressure, and, after removal of unchanged

2-amino-4-hydroxyquinoline (1 g., 6%) by extraction of the residue with sodium hydroxide, *2-amino-4-methoxyquinoline* was obtained as plates (12·3 g., 71%), m. p. 195—196°, by crystallisation of the alkali-insoluble material from benzene (Found: C, 68·6; H, 5·8; N, 16·2. $C_{10}H_{10}ON_2$ requires C, 68·9; H, 5·8; N, 16·1%). Its *benzenesulphonate* separated from *iso*propyl alcohol in prisms, m. p. 203—204° (Found: C, 58·0; H, 4·9; N, 8·3. $C_{16}H_{16}O_4N_2S$ requires C, 57·8; H, 4·9; N, 8·4%). The yield in this preparation fell markedly with any decrease in the quantity of diazomethane.

2-Amino-4-ethoxyquinoline.—A suspension of the silver salt [prepared from 2-amino-4-hydroxyquinoline (12 g.), sodium (2·3 g., 1·3 g.-atoms), and silver nitrate (17 g., 1·3 mol.)] in aqueous ethanol (250 ml.) was boiled with ethyl bromide (22 g., 2·7 mols.), added gradually during 18 hr. The suspension was filtered, and the crude base, obtained by evaporation of the filtrate and treatment of the residue with sodium hydroxide, afforded the *benzenesulphonate* on the addition of aqueous-ethanolic benzenesulphonic acid; it formed needles (9·8 g., 38%), m. p. 229°, from *iso*propyl alcohol (Found: C, 59·1; H, 5·2; N, 8·0. $C_{17}H_{18}O_4N_2S$ requires C, 59·0; H, 5·2; N, 8·1%). *2-Amino-4-ethoxyquinoline* crystallised from benzene as plates, m. p. 164—165° (Found: C, 70·6; H, 6·1; N, 14·7. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4; N, 14·9%). A solution of 2-amino-4-ethoxyquinoline (3 g.) in aqueous hydrobromic acid (48%; 30 ml.) was boiled for 3 hr., distilled to remove most of the acid, and made alkaline to Titan-yellow with aqueous sodium hydroxide; the clear solution, on being neutralised with hydrochloric acid, afforded 2-amino-4-hydroxyquinoline (2·2 g., 86%), which, after recrystallisation from water, had m. p. and mixed m. p. 300—302° (decomp.). Its picrate had m. p. 263—265° (decomp.), undepressed by an authentic specimen (Part II, *loc. cit.*).

The following ethers and their salts were prepared in a similar manner:

2-Amino-4-n-propoxyquinoline, needles, m. p. 142—142·5°, from benzene (Found: C, 71·3; H, 7·4; N, 13·6. $C_{12}H_{14}ON_2$ requires C, 71·3; H, 7·0; N, 13·9%); yield 65%. *Benzenesulphonate*, prisms, m. p. 191·5—192·5°, from ethanol (Found: C, 60·1; H, 5·9; N, 7·9. $C_{18}H_{20}O_4N_2S$ requires C, 60·0; H, 5·6; N, 7·8%).

2-Amino-4-isopropoxyquinoline, prisms (61%), m. p. 140°, from benzene (Found: C, 70·9; H, 6·8; N, 13·7%). *Benzenesulphonate*, prisms, m. p. 212°, from ethanol (Found: C, 60·2; H, 5·7; N, 7·8%).

2-Amino-4-n-butoxyquinoline, needles (46%), m. p. 167—169°, from light petroleum (b. p. 100—120°) (Found: C, 71·9; H, 7·2; N, 13·2. $C_{13}H_{16}ON_2$ requires C, 72·2; H, 7·5; N, 13·0%). *Benzenesulphonate*, prisms, m. p. 175—176°, from ethanol (Found: C, 60·9; H, 6·1; N, 7·7. $C_{19}H_{22}O_4N_2S$ requires C, 61·0; H, 5·9; N, 7·5%). *Nitrate*, needles, m. p. 172—173°, from *iso*propyl alcohol (Found: C, 56·0; H, 6·4; N, 15·1. $C_{13}H_{17}O_4N_3$ requires C, 55·9; H, 6·1; N, 15·1%).

2-Amino-4-n-pentyloxyquinoline, needles (74%), m. p. 141—142°, from benzene (Found C, 72·8; H, 7·6; N, 12·2. $C_{14}H_{18}ON_2$ requires C, 73·0; H, 7·9; N, 12·2%). *Benzenesulphonate*, needles, m. p. 166·5—167°, from ethanol (Found: C, 61·9; H, 6·1; N, 7·3. $C_{20}H_{24}O_4N_2S$ requires C, 61·8; H, 6·2; N, 7·2%).

2-Amino-4-1'-methylbutoxyquinoline, needles (37%), m. p. 101—102°, from *cyclo*hexanol (Found: C, 72·7; H, 7·9; N, 12·3. $C_{14}H_{18}ON_2$ requires C, 73·0; H, 7·9; N, 12·2%). *Benzenesulphonate*, cubes, m. p. 191—191·5°, from *iso*propyl alcohol (Found: C, 62·2; H, 5·9; N, 7·4. $C_{20}H_{24}O_4N_2S$ requires C, 61·8; H, 6·2; N, 7·2%).

2-Amino-4-n-octyloxyquinoline, needles (63%), m. p. 128—129°, from *cyclo*hexanol (Found: C, 75·0; H, 9·1; N, 10·4. $C_{17}H_{24}ON_2$ requires C, 75·0; H, 8·9; N, 10·3%). *Benzenesulphonate*, needles, m. p. 145—146°, from *iso*propyl alcohol (Found: C, 64·3; H, 7·1; N, 6·5. $C_{23}H_{30}O_4N_2S$ requires C, 64·2; H, 7·0; N, 6·5%).

1:3-Bis-(2-aminoquinolyl-4-oxy)propane, prisms (49%), m. p. 256—258° (decomp.), from aqueous ethanol (Found: C, 70·1; H, 5·8; N, 15·2. $C_{21}H_{20}O_2N_4$ requires C, 70·0; H, 5·6; N, 15·5%). *Dibenzenesulphonate*, needles, m. p. 227·5—228·5° (decomp.), from ethanol (Found: loss at 110°/vac., 6·8; C, 57·8; H, 5·0; N, 7·7. $C_{33}H_{32}O_8N_4S_2,C_2H_6O$ requires C_2H_6O, 6·4; C, 58·1; H, 5·3; N, 7·7%).

2-Benzamido-4-methoxyquinoline.—Anhydrous 2-amino-4-methoxyquinoline (2·1 g.) was boiled for 5 hr. in benzene (50 ml.) with benzoyl chloride (2·1 g., 1·25 mols.) in the presence of triethylamine (3 g., 2·5 mols.). The suspension was evaporated to dryness and the residue, after crystallisation first from aqueous ethanol and then from ether, afforded the *benzoyl* derivative as prisms, m. p. 77—81° (1·4 g., 42%) (Found: N, 9·9. $C_{17}H_{14}O_2N_2$ requires N, 10·1%).

2-p-Anisamido-4-methoxyquinoline, prepared in a similar manner, crystallised from aqueous

ethanol as needles, m. p. 133—134°; yield 84% (Found: N, 9·1. $C_{18}H_{16}O_3N_2$ requires N, 9·1%). Unchanged 2-amino-4-methoxyquinoline was recovered when the acylation was attempted under Schotten–Baumann conditions.

4-Methoxy-2-piperonamidoquinoline occurred as needles (75%), m. p. 187·5°, when crystallised from ethanol (Found: C, 66·8; H, 4·3; N, 8·5. $C_{18}H_{14}O_4N_2$ requires C, 67·1; H, 4·4; N, 8·7%).

2-(3 : 4-Dimethoxybenzamido)-4-methoxyquinoline separated as needles (97%), m. p. 154°, from ethanol (Found: C, 67·5; H, 5·4; N, 8·6. $C_{19}H_{18}O_4N_2$ requires C, 67·4; H, 5·4; N, 8·3%).

2-Diphenylacetamido-4-methoxyquinoline was obtained as prisms (77%), m. p. 156—157°, from methanol (Found: C, 78·4; H, 5·1; N, 7·6. $C_{24}H_{20}O_2N_2$ requires C, 78·2; H, 5·5; N, 7·6%).

4-Methoxy-2-phenylacetamidoquinoline crystallised from ethanol as plates (66%), m. p. 245—246° (decomp.) (Found: C, 73·9; H, 5·6; N, 9·7. $C_{18}H_{16}O_2N_2$ requires C, 74·0; H, 5·5; N, 9·6%). When the acylation was effected in pyridine solution and in aqueous sodium hydroxide, the yields were 14% and 31% respectively.

2-Acetamido-4-hydroxyquinoline.—(i) Anhydrous 2-amino-4-hydroxyquinoline (4 g.) was boiled for 30 min. with acetic anhydride (5·5 g., 2 mols.) in glacial acetic acid (6 ml.) containing concentrated sulphuric acid (2 drops). The mixture was poured into water and the precipitated *acetyl* derivative crystallised as needles (3·7 g., 73%), m. p. 302—303° (decomp.), from dilute acetic acid (Found in material dried at 150°/vac.: C, 65·3; H, 5·1; N, 13·9. $C_{11}H_{10}O_2N_2$ requires C, 65·3; H, 5·0; N, 13·9%). This compound was soluble in aqueous sodium hydroxide and gave the same colour as does 2-amino-4-hydroxyquinoline with ferric chloride.

(ii) When the aminoquinoline (4 g.) was boiled for 3 hr. with acetyl chloride (6·4 g., 3·3 mols.) in pyridine (60 ml.) containing piperidine (2 drops), the *hydrochloride* of the acetyl derivative was obtained; it formed needles, m. p. 315—317° (decomp.) (5·3 g., 89%), from water (Found: C, 55·7; H, 4·6. $C_{11}H_{11}O_2N_2Cl$ requires C, 55·4; H, 4·6%). A sample of the base, m. p. 302—303° (decomp.), recovered from the hydrochloride did not depress the m. p. of the foregoing base. Acetylation could not be effected either in the absence of sulphuric acid or by Chattaway's method (*J.*, 1931, 2495).

2-Acetamido-4-methoxyquinoline was prepared (i) in 93% yield by acetylation of the aminoquinoline in the presence of sulphuric acid and (ii) in 80% yield by methylation of 2-acetamido-4-hydroxyquinoline (0·55 g.) in methanol (40 ml.) with diazomethane obtained from nitrosomethylurea (7 g.); it formed plates, m. p. 250—251°, from ethanol (Found: N, 12·9. $C_{12}H_{12}O_2N_2$ requires N, 13·0%).

2-Amino-4 : 6-dimethoxyquinoline was prepared by treatment of 2-amino-4 : 6-dihydroxyquinoline with diazomethane and crystallised from benzene as plates, m. p. 188·5—189° (43%) (Found: C, 64·7; H, 5·8; N, 14·1. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9; N, 13·7%). From the mother-liquors 2-amino-4-hydroxy-6-methoxyquinoline, m. p. and mixed m. p. 293—295° (decomp.), was isolated in 32% yield.

2-Amino-4 : 6-dihydroxyquinolinium bromide (yield 92%) separated when 2-amino-4-hydroxy-6-methoxyquinoline was boiled for 7 hr. with hydrobromic acid; on recrystallisation from glacial acetic acid, this salt was obtained as needles, m. p. 280—281° (decomp.) (Found: C, 41·8; H, 3·8. $C_9H_9O_2N_2Br$ requires C, 42·0; H, 3·5%). The m. p. of the base prepared from the bromide was undepressed on admixture with an authentic specimen (Part II, *loc. cit.*).

2-Amino-4 : 8-dihydroxyquinoline, prepared in 95% yield by demethylation of the corresponding 8-methoxyquinoline with hydriodic acid, was isolated as its *hydrochloride* which crystallised as hygroscopic needles, m. p. 301—302° (decomp.), from dilute hydrochloric acid (Found, in material dried at 150°/vac.: N, 13·4. $C_9H_9O_2N_2Cl$ requires N, 13·2%). Its *picrate* crystallised from aqueous ethanol as yellow prisms, m. p. 253—255° (decomp.) (Found: C, 44·3; H, 3·0. $C_{15}H_{11}O_9N_5$ requires C, 44·4; H, 2·7%). This demethylation could not be effected with aqueous hydrobromic acid (48%) or with hydrobromic acid (55%) in glacial acetic acid.

2-Amino-4 : 8-dihydroxy-5-methylquinoline.—The 8-methoxyquinoline was boiled with hydriodic acid for 12 hr. and the solution was evaporated to dryness. On addition of hydrochloric acid to an aqueous extract of the residue the *hydrochloride* separated in 95% yield; it gave prisms, m. p. 333—334° (decomp.), from ethanol (Found: C, 53·2; H, 5·1. $C_{10}H_{11}O_2N_2Cl$ requires C, 53·0; H, 4·9%). Its *picrate* was obtained as yellow needles, m. p. 268° (decomp.), from aqueous ethanol (Found: C, 46·2; H, 3·1. $C_{16}H_{12}O_9N_5$ requires C, 45·8; H, 3·1%).

Interaction of EthylCyanoacetate and o-Hydroxyanilinium Benzenesulphonate.—The nitrile

(22·6 g.) and the salt (53·4 g., 1 mol.) reacted exothermically when heated at 180° for 1 hr. Ammonium benzenesulphonate (23·4 g., 67%) remained undissolved when the cooled melt was extracted with chloroform. The chloroform extract on distillation afforded 2-methylbenzoxazole (6 g., 22%), b. p. 200—201° (Ladenburg, *Ber.*, 1876, **9**, 1524, records b. p. 200—201°). It was further characterised by conversion into *o*-hydroxyacetanilide, m. p. and mixed m. p. 209°. By crystallisation of the non-volatile residue from ethanol, *oo'-dihydroxymalondianilide* (4·8 g., 17%) was obtained as plates, m. p. 233·5—234·5° (decomp.) [Found: C, 63·1; H, 4·5; N, 9·8%; *M* (Rast), 266. $C_{15}H_{14}O_4N_2$ requires C, 62·9; H, 4·9; N, 9·8%; *M*, 286].

o-Hydroxyanilinium benzenesulphonate, needles from equal volumes of ethanol and ethyl acetate, had m. p. 237—238° (decomp.) (Found: N, 5·3. $C_{12}H_{13}O_4NS$ requires N, 5·2%).

Interaction of 2-Amino-4-n-butoxyquinoline and Nitrous Acid.—(i) A suspension of 2-amino-4-*n*-butoxyquinoline (6·5 g.) in concentrated hydrochloric acid was treated at 0° with sodium nitrite (4·1 g.); after being kept overnight at 0°, there was added further sodium nitrite (2 g.) and the mixture was warmed on a steam-bath for 10 min. The precipitate afforded *4-n-butoxy-2-hydroxyquinoline*, m. p. 184—185° (5·1 g., 78%), as prisms on crystallisation from aqueous ethanol (Found: C, 72·0; H, 7·2; N, 6·7. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 7·0; N, 6·5%). *4-n-Butoxy-2-chloroquinoline* (1·35 g., 19%), liberated from the mother-liquors, crystallised as prisms, m. p. 88—89°, from aqueous methanol (Found: C, 66·5; H, 6·3; N, 5·8; Cl, 14·6. $C_{13}H_{14}ONCl$ requires C, 66·3; H, 6·0; N, 6·0; Cl, 15·1%).

A solution of 4-*n*-butoxy-2-hydroxyquinoline (1 g.) in aqueous hydrobromic acid (48%; 30 ml.) was distilled at atmospheric pressure until 25 ml. of distillate, which contained butyl bromide, had been collected. The residue was made alkaline to Titan-yellow with aqueous sodium hydroxide, filtered, and neutralised with hydrochloric acid. The precipitated 2 : 4-dihydroxyquinoline (0·3 g.), m. p. 352—354° (decomp.), was characterised as its acetyl derivative, m. p. 213—214°, undepressed by an authentic specimen (Ashley, Perkin, and Robinson, *J.*, 1930, 382).

(ii) 2-Amino-4-*n*-butoxyquinoline (5 g.), dissolved in concentrated sulphuric acid (10 ml.) and treated with sodium nitrite in the usual way, furnished the 2-hydroxyquinoline (4 g., 80%), m. p. and mixed m. p. 184—185°.

2-Amino-3-bromo-4-hydroxyquinoline.—2-Amino-4-hydroxyquinoline (2 g.), dissolved in glacial acetic acid (32 ml.), was treated during 10 min. at the b. p. with bromine (2 g., 1 mol.) dissolved in glacial acetic acid (5 ml.); boiling was continued for 30 min. Next day, the *2-amino-3-bromo-4-hydroxyquinolinium bromide* (3·7 g., 93%) was collected; it formed needles, m. p. 249—252° (decomp.), unchanged after recrystallisation from glacial acetic acid (Found: N, 9·0. $C_9H_8ON_2Br_2$ requires N, 8·8%). The *base* crystallised from aqueous ethanol as rods, m. p. 280—281° (decomp.) (Found: N, 11·9. $C_9H_7ON_2Br$ requires N, 11·7%). Its *picrate* separated as yellow elongated prisms, m. p. 244—245° (decomp.), from ethanol (Found: N, 15·2. $C_{15}H_{10}O_8N_5Br$ requires N, 15·0%).

3-Bromo-2 : 4-dihydroxyquinoline.—(i) The crude product which separated when 2-amino-3-bromo-4-hydroxyquinoline (12 g.) was dissolved in concentrated sulphuric acid (25 ml.), treated with sodium nitrite (12 g., 3·5 mols.) at 0° during 20 min., allowed to warm to room temperature, and poured on crushed ice furnished *3-bromo-2 : 4-dihydroxyquinoline* as plates, m. p. 231—232° (decomp.), on crystallisation from glacial acetic acid (Found: C, 44·8; H, 3·1; N, 5·7; Br, 33·0. $C_9H_6O_2NBr$ requires C, 45·0; H, 2·5; N, 5·8; Br, 33·3%); yield 10 g. (83%). Its *monoacetate* crystallised as needles, m. p. 228—229° (decomp.), from methanol (Found: C, 46·6; H, 3·2. $C_{11}H_8O_3NBr$ requires C, 46·8; H, 2·8%).

(ii) 2 : 4-Dihydroxyquinoline (1 g.), treated with bromine (1 g., 1 mol.) in the manner described for 2-amino-3-bromo-4-hydroxyquinoline, yielded 3-bromo-2 : 4-dihydroxyquinoline (1·35 g., 90%), m. p. and mixed m. p. 232—233° (decomp.) (Found: N, 5·6. Calc. for $C_9H_6O_2NBr$: N, 5·8%). The acetate prepared from this material had m. p. and mixed m. p. 228—229° (decomp.).

(iii) 2 : 4-Dihydroxyquinoline (2 g.), dissolved in formic acid (98—100%; 30 ml.), was treated with a solution of bromine (2 g., 1 mol.) in formic acid (12 ml.) as described for 2-amino-3-bromo-4-hydroxyquinoline. By fractional crystallisation of the crude product (2·65 g.; m. p. 180—190°) from methanol, there were obtained 3-bromo-2 : 4-dihydroxyquinoline, m. p. and mixed m. p. 232—234° (decomp.) (Found: N, 5·5; Br, 33·6. Calc. for $C_9H_6O_2NBr$: N, 5·8; Br, 33·3%), and a *dibromo-2 : 4-dihydroxyquinoline*, needles, m. p. 276—278° (decomp.), from methanol (Found: C, 34·1; H, 1·9; N, 4·3; Br, 51·2. $C_9H_5O_2NBr_2$ requires C, 33·9; H, 1·6; N, 4·4; Br, 50·2%). The *acetate* of the dibromo-derivative crystallised as needles,

m. p. 254° (decomp.), from glacial acetic acid (Found : N, 4·0; Br, 45·0. $C_{11}H_7O_3NBr_2$ requires N, 3·9; Br, 44·3%).

Oxidation of 2 : 4-*Dihydroxyquinoline.*—2 : 4-Dihydroxyquinoline (5 g.), dissolved in aqueous sodium hydroxide (10%, 50 ml.), was treated at 80—85° with saturated aqueous potassium permanganate (200 ml.). The filtrate from the manganese dioxide was adjusted to pH 6 and unchanged 2 : 4-dihydroxyquinoline (1·45 g.) was removed; the methanol-soluble fraction of the water-soluble material, when warmed in acid solution, furnished isatin (1·85 g., 41%), m. p. and mixed m. p. 200—201°.

Oxidation of 3-*Bromo*-2 : 4-*dihydroxyquinoline.*—3-Bromo-2 : 4-dihydroxyquinoline (6 g.), oxidised with saturated aqueous potassium permanganate (300 ml.) in alkaline solution as described in the foregoing experiment, afforded crude isatin (1·2 g., 33%) which after two recrystallisations from ethanol had m. p. and mixed m. p. 199—200°.

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Some Reactions of Ethyl Cyanoacetate.

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The action of *N*-bromosuccinimide on ethyl cyanoacetate yields ethyl dibromocyanoacetate, which is also obtained together with dibromoacetonitrile by the action of bromine in the presence of magnesium oxide, the proportions of the products being dependent upon the amount of magnesium oxide used. Oxidation of ethyl cyanoacetate by selenium dioxide gives diethyl *trans*(?)-1 : 2-dicyanoethylene-1 : 2-dicarboxylate.

IN unsuccessful attempts to prepare ethoxalyl cyanide, $EtO_2C{\cdot}CO{\cdot}CN$, or a derivative of this (see also Diels, Gärtner, and Kaack, *Ber.*, 1922, **55**, 3439), a number of reactions of ethyl cyanoacetate has been studied.

Ethyl dibromocyanoacetate has been prepared for the first time and is best obtained by the reaction of *N*-bromosuccinimide (2 mols.) with ethyl cyanoacetate (1 mol.) in carbon tetrachloride solution. Photocatalysed bromination of ethyl cyanoacetate in organic solvents by bromine (2 mols.) was incomplete and the product decomposed during washing to remove unchanged bromine. Bromination by bromine (2 mols.) in aqueous solution in the presence of magnesium oxide (1 mol., as acid absorbent) led to the reaction of the magnesium oxide completely after the addition of only one mol. of bromine, and carbon dioxide was evolved during the subsequent addition of the second mol. The product on fractionation gave ethyl dibromocyanoacetate and dibromoacetonitrile in approximately equimolecular amounts. When magnesium oxide (2 mols.) was used, and the reaction was completed by acidification after the addition of the bromine, the product was predominantly dibromoacetonitrile and this offers an easy route to the latter compound, previously obtained by dehydration of dibromoacetamide by phosphoric oxide (Steinkopf, *Ber.*, 1905, **38**, 2695; Ghigi, *Gazzetta*, 1941, **71**, 641).

Several attempts were made to replace the bromine atoms in ethyl dibromocyanoacetate, but treatment with alkaline reagents, *e.g.*, sodium ethoxide in ethanol, or ethanolic potassium acetate, led to rapid darkening of the mixture, and only small amounts of unidentified volatile liquid products could be separated from the large amounts of tar formed. This behaviour in the presence of alkaline reagents accounts for the decomposition during the washing to remove bromine left after the photobromination experiments.

In view of recent observations by Mel'nikov and Baskakov (*Doklady Akad. Nauk S.S.S.R.*, 1952, **85**, 337; *Chem. Abs.*, 1953, **47**, 7461) on the oxidation of nitriles by selenium dioxide, it is unlikely that ethoxalyl cyanide, if formed by the action of selenium dioxide on ethyl cyanoacetate, would survive in the reaction mixture. Selenium dioxide reacted

with ethyl cyanoacetate in ethanol at 100°, but the product was a seleniferous material, largely undistillable. When selenium dioxide was heated with ethyl cyanoacetate alone at 120—125° [the conditions used by Astin, Newman, and Riley (*J.*, 1933, 391) for the comparable oxidation of ethyl malonate to ethyl mesoxalate] and the product was distilled, two fractions were obtained, the larger of which was unchanged ethyl cyanoacetate, contaminated with selenium compounds. The second fraction was a solid, $(C_5H_5O_2N)_x$, m. p. 117—117·5°, which corresponds closely with the m. p. recorded for triethyl 1 : 2 : 3-tricyano-*cyclo*propane-1 : 2 : 3-tricarboxylate. The latter had been prepared by, *inter al.*, Errera and Perciabosco (*Ber.*, 1901, **34**, 3708) in variable yield by the reaction of bromine, iodine, or ethyl monobromocyanoacetate upon ethyl sodiocyanoacetate in ether. In the present study, when all the sodium was made to react with ethyl cyanoacetate before the addition of the bromo-ester, none of the *cyclo*propane ester was formed but, when free sodium was present, this ester was obtained and this result, taken together with the difficulty found in causing complete reaction of the metal with the ester, probably explains the variable yields reported by the earlier workers; the *cyclo*propane ester melted at 123·5—124°, but its mixed m. p. with the product, $(C_5H_5O_2N)_x$, was 99—99·5°. Prolonged hydrolysis of the compound with 6N-potassium hydroxide solution gave ammonia, but no product could be isolated. The compound was recovered unchanged when treated with ethanolic hydrogen chloride, either in the cold or under reflux, and with ethanolic sulphuric acid (approx. 5N) at 210°. A small amount was also recovered from an attempted reaction between it and ethanolic sulphuric acid (5N) at 170° but the main product was an oil, probably a mixture of two or more compounds.

With ethanolic hydrazine hydrate, the compound of m. p. 117—117·5° readily formed a dihydrazide. A molecular-weight determination on the original compound showed $x = 2$; therefore the action of selenium dioxide on ethyl cyanoacetate yields diethyl 1 : 2-dicyanoethylene-1 : 2-dicarboxylate. Treatment of the compound with magnesium *n*-propoxide in *n*-propanol (Linstead and Whalley, *J.*, 1952, 4839) did not yield any tetra-azaporphin-like pigment and on this account the geometric configuration is thought, provisionally, to be *trans*.

Experimental

Ethyl Dibromocyanoacetate.—(*a*) Ethyl cyanoacetate (33·9 g.) in carbon tetrachloride (300 ml.) was heated under reflux with *N*-bromosuccinimide (106·8 g.) and benzoyl peroxide (0·5 g.) for 16 hr. Succinimide was removed by filtration, the solvent evaporated, and the residue distilled, yielding *ethyl dibromocyanoacetate* as a colourless liquid (73 g.), b. p. 70—72°/1·3 mm., n^{18} 1·4957 (Found: C, 22·1; H, 2·1; N, 5·2; Br, 59·1. $C_5H_5O_2NBr_2$ requires C, 22·1; H, 1·85; N, 5·2; Br, 59·0%).

(*b*) Ethyl cyanoacetate (56·6 g.) was stirred with water (350 ml.), in which was suspended magnesium oxide (21 g.), while bromine (160 g., 2 mols.) was added dropwise. After addition of half the volume of bromine, all the magnesium oxide had dissolved and effervescence (CO_2) became pronounced. The mixture was kept overnight, the oil separated, and the aqueous residue extracted with carbon tetrachloride. The combined oil and carbon tetrachloride solution were washed with sodium carbonate and sodium thiosulphate solutions successively and dried ($MgSO_4$). The solvent was evaporated, and the residue fractionally distilled through a Vigreux column (10 cm.), to yield dibromoacetonitrile (35·1 g.), b. p. 30°/1·6 mm., n^{18} 1·5429 (Ghigi, *loc. cit.*, gives b. p. 67—69°/20 mm.) (Found: C, 12·1; H, 0·55; N, 6·9; Br, 80·5. Calc. for C_2HNBr_2: C, 12·1; H, 0·5; N, 7·0; Br, 80·4%), and ethyl dibromocyanoacetate (44·8 g.), b. p. 76—77°/2 mm., n^{18} 1·4960.

Dibromoacetonitrile.—Ethyl cyanoacetate (56·6 g.), magnesium oxide (42 g.), and water (350 ml.) were stirred together at room temperature, while bromine (160 g.) was added dropwise. At the end of the addition the mixture was acidified with concentrated hydrochloric acid (Congo-red), carbon dioxide being evolved. The solution was extracted with carbon tetrachloride, and the extract washed successively with sodium carbonate and sodium thiosulphate solutions and dried ($MgSO_4$). The solvent was evaporated and the residue was fractionally distilled, yielding dibromoacetonitrile (58·2 g.), b. p. 68—70°/20 mm., and ethyl dibromocyanoacetate (8·4 g.), b. p. 120—123°/20 mm.

Diethyl trans(?)-1 : 2-*Dicyanoethylene*-1 : 2-*dicarboxylate.*—A mixture of ethyl cyanoacetate (50 g.) and selenium dioxide (25 g.) was heated under reflux at 120—125° in an oil-bath for 2 hr.,

during which the mixture effervesced and selenium separated. When cool, the liquid was decanted from the selenium residues and fractionally distilled. The major fraction (31·1 g.), b. p. 86—94°/12 mm., smelled strongly of selenium compounds and was identified as impure ethyl cyanoacetate by conversion into cyanoacetamide, m. p. and mixed m. p. 119—120°. The fraction (6·8 g.), b. p. 120—200°/12 mm., solidified when cool and crystallised from ethanol, to yield *diethyl* 1 : 2-*dicyanoethylene*-1 : 2-*dicarboxylate* as colourless needles, m. p. 117—117·5° (corr.) [Found: C, 54·4; H, 4·6; N, 12·7%; *M* (Rast), 226. $C_{10}H_{10}O_4N_2$ requires C, 54·05; H, 4·5; N, 12·6%; *M*, 222]. The compound decolorised bromine water on being heated, and slowly liberated ammonia in boiling 6N-potassium hydroxide. The *dihydrazide*, prepared by using hydrazine hydrate (100%) in ethanol, crystallised from 95% ethanol as flat needles, m. p. 211·5° (decomp.) (Found: C, 40·0, 39·9; H, 5·0, 5·1; N, 34·6. $C_6H_8O_2N_6,C_2H_5{\cdot}OH$ requires C, 40·0; H, 5·0; N, 35·0%). When heated in a vacuum in an attempt to remove solvent, the compound sublimed.

Triethyl 1 : 2 : 3-*Tricyanocyclopropane*-1 : 2 : 3-*tricarboxylate*.—Sodium wire (6 g.) in dry ether (100 ml.) was treated with ethyl cyanoacetate (29 g.). Next day, when only some of the sodium had reacted, ethyl monobromocyanoacetate (50·8 g.) was added, and the mixture kept with intermittent shaking for 2 days. The product, isolated as described by Errera and Perciabosco (*loc. cit.*), crystallised from ethanol to yield colourless needles (7·5 g.), m. p. 123·5—124° (corr.) (Errera and Perciabosco, *loc. cit.*, give m. p. 119·5; Goldthwaite, *Amer. Chem. J.*, 1903, **30**, 465, gives 122°); mixed m. p. with the ethylene (above), 99—99·5° [Found: C, 54·4; H, 4·5; N, 12·8%; *M* (Rast), 340. Calc. for $C_{15}H_{15}O_6N_3$: C, 54·05; H, 4·5; N, 12·6%; *M*, 333]. The compound did not decolorise bromine water even when heated.

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The Structure of Bacterial Polyglutamic Acid.

By S. G. WALEY.

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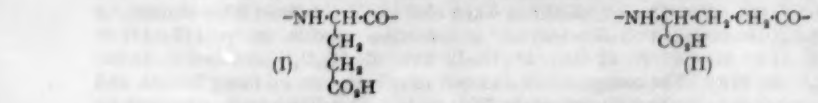
Poly-(γ-L-glutamyl)-L-glutamic acid has been synthesised. Condensation of *N*-benzyloxycarbonyl-γ-L-glutamyl azide with γ-benzyl L-glutamate gave γ-benzyl *N*-(benzyloxycarbonyl-γ-L-glutamyl)-L-glutamate, which was esterified and then hydrogenated to α-methyl *N*-(α-methyl γ-L-glutamyl)-L-glutamate (III). Polymerisation with tetraethyl pyrophosphite (Anderson, Blodinger, and Welcher, *J. Amer. Chem. Soc.*, 1952, **74**, 5309), followed by hydrolysis gave the γ-linked poly-L-glutamic acid. Comparison of its properties with those of the poly-D-glutamic acids from *B. anthracis* (Hanby and Rydon, *Biochem. J.*, 1946, **40**, 297) and from *B. licheniformis* (Bovarnick, Eisenberg, O'Connell, Victor, and Owades, *J. Biol. Chem.*, 1954, **207**, 593) showed that the naturally occurring compound was also γ-linked.

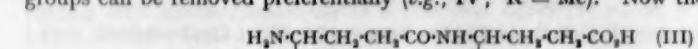
AMONG the many known natural products built up from amino-acid residues there is one that is structurally unique, in that its molecular weight is as large as that of a protein though its structure much simpler. This is poly-D-glutamic acid, formed by certain bacteria of the genus *Bacillus*, such as *B. anthracis* and *B. licheniformis*. The polypeptide is readily purified and on hydrolysis furnishes only D-glutamic acid (Hanby and Rydon, *Biochem. J.*, 1946, **40**, 297; Pongor, *Experientia*, 1950, **6**, 421; see also Bricas and Fromageot, *Adv. Protein Chem.*, 1953, **8**, 64, for a general review of the literature on poly-D-glutamic acid). So the main structural interest centres on whether the glutamyl residues are α-linked (I) or γ-linked (II), or whether both types of linkage are present; this is also, of course, a general problem in protein chemistry whenever glutamyl or aspartyl residues

are encountered (Quastel, Stewart, and Tunnicliffe, *Biochem. J.*, 1923, **17**, 591; Kandel, Kandel, Kovács, and Bruckner, *Naturwiss.*, 1954, **41**, 281). Bovarnick (*J. Biol. Chem.*, 1942, **145**, 415) suggested that the polypeptide from *B. licheniformis* was γ-linked (II) on

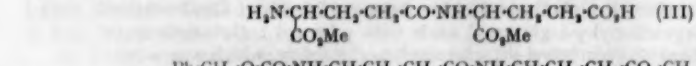


the grounds that it does not give the biuret test and was not racemised by alkali. Hanby and Rydon (*loc. cit.*) inferred the presence of γ-peptide links in the polypeptide from *B. anthracis* from the increase of apparent amino-nitrogen content with the time of reaction with nitrous acid; Sachs and Brand (*J. Amer. Chem. Soc.*, 1954, **76**, 3601) have recently shown that γ-glutamyl peptides with free α-amino- and α-carboxyl groups liberate nearly all their nitrogen in the Van Slyke reaction, with formation of the lactone of α-hydroxyglutaric acid; the relatively slow and incomplete evolution of nitrogen from the polypeptide may result from the low concentration of end groups, or from side reactions in the stepwise degradation. This complicated reaction gives no information on the number of γ-peptide links present. Hanby and Rydon interpreted titration curves as indicating that the polypeptide was predominantly α-linked (I); it now seems likely that they were misled by choosing too low a value for the pK of the α-carboxyl group of a glutamyl residue. Bruckner, Kovács, and their co-workers, on the other hand, produced evidence that the polypeptide was entirely γ-linked (II) (*J.*, 1952, 4255; 1953, 145, 149, 1512; *Nature*, 1953, **172**, 508); they converted methyl poly-D-glutamate into the amide (or hydrazide) and submitted it to Hofmann (or Curtius) degradation: β-formylpropionic acid was the only product isolated. An α-linked polyglutamic acid (I) had already been synthesised (Hanby, Waley, and Watson, *J.*, 1950, 3239) and several of its properties found to differ from those of the natural product; the γ-linked isomer (II) has now been prepared; a preliminary account of this work has been given (Waley, *Chem. and Ind.*, 1954, 1149).

The synthesis of a γ-linked polyglutamic acid presents several problems: direct polymerisation of α-methyl glutamate is out of the question as preferential cyclisation to methyl 5-oxopyrrolidine-2-carboxylate would occur. So it is necessary to prepare a γ-linked dipeptide with both the α-carboxyl groups suitably protected (*e.g.*, III); further this must be formed from a precursor in which the protective groups on the amino- and the γ-carboxyl groups can be removed preferentially (*e.g.*, IV; R = Me). Now the γ-carboxyl group of



(III)



(IV)

glutamic acid can be preferentially esterified and this is the basis of the scheme chosen: γ-methyl L-glutamate was converted into benzyloxycarbonyl-γ-L-glutamylhydrazide (by a somewhat simplified method) and the azide condensed with γ-benzyl L-glutamate by the method of Boothe *et al.* (*J. Amer. Chem. Soc.*, 1949, **71**, 2304) to give a satisfactory yield of γ-benzyl *N*-(benzyloxycarbonyl-γ-L-glutamyl)-L-glutamate (IV; R = H). Under some conditions benzyloxycarbonyl-γ-L-glutamyl azide gives a mixture of α- and γ-linked peptides (Sachs and Brand, *J. Amer. Chem. Soc.*, 1954, **76**, 1815), but only the γ-linked product was obtained in this case, as shown by hydrogenation to γ-L-glutamyl-L-glutamic acid, free from the α-isomer. Esterification with diazomethane gave the dimethyl ester (IV; R = Me), from which hydrogenation removed the benzyl ester and benzyloxycarbonyl groups to give the dipeptide (III). An earlier attempt to obtain the ester (IV; R = Me) required α-benzyl α-methyl L-glutamate: no pure product could be isolated after treatment of crude γ-benzyl α-methyl-*N*-formyl-L-glutamate with hydrogen chloride in benzyl alcohol (cf. Waley, *Chem. and Ind.*, 1953, 107), and the formyl derivative itself was not obtained pure.

Several ways of polymerising peptides have been examined (Frankel, Liwschitz, and

Zilkha, *Experientia*, 1953, **9**, 179; Wieland and Bernhard, *Annalen*, 1953, **582**, 218; Noguchi and Hayakawa, *J. Amer. Chem. Soc.*, 1954, **76**, 2846) but in general only very low degrees of polymerisation were achieved. Although some polymeric material was obtained by the action of phosphorus trichloride in pyridine on the dipeptide (III) (cf. Goldschmidt and Lautenschlager, *Annalen*, 1953, **580**, 68) the polypeptide was contaminated with a phosphorus-containing polymer; γ-linked poly-L-glutamic acid was obtained pure, however, by heating the dipeptide (III) with tetraethyl pyrophosphite in diethyl phosphite (Anderson, Blodinger, and Welcher, *J. Amer. Chem. Soc.*, 1952, **74**, 5309), followed by brief hydrolysis with cold, dilute alkali; the ready hydrolysis of esters of the naturally occurring poly-D-glutamic acid was already known (Fraenkel-Conrat and Olcott, *J. Biol. Chem.*, 1945, **161**, 259). Detailed comparison of this synthetic poly-L-glutamic acid with the poly-D-glutamic acids (from *B. anthracis* and *B. licheniformis*) showed that the latter were, indeed, γ-linked.

The infrared spectra of the synthetic γ-linked and α-linked polypeptides differed: the most prominent of the peaks not shared by both isomers were at 8·25, 8·88, and 9·80 μ in the γ-linked one, and at 7·12, 7·90, 8·58, and 12·70 μ in the α-linked one. Most of these peaks are in the skeletal region, but the peak at 8·25 μ (in the γ-linked isomer) is present in acylamino-acids and is assigned to the carboxyl group; the environment of this group is closer to that in an acylamino-acid in (II) than it is in (I). Clayton and Kenner (*Chem. and Ind.*, 1953, 1205) noted a shift in the carbonyl-stretching band of the carboxyl group (5·84 to 4·77 μ) in the conversion of an α-glutamyl peptide into a γ-glutamyl one. For polyglutamic acids, however, the peak in this region (5·82 μ) is common to both isomers. The poly-D-glutamic acid from *B. licheniformis* had an infrared absorption curve very similar to the synthetic γ-linked polypeptide and, although the curve of the product from *B. anthracis* was poorly resolved, it clearly belonged to the γ-linked type.

The partial hydrolysis of poly-D-glutamic acid had not previously been studied; it was found that hydrolysis in constant-boiling hydrobromic acid at 100° was rapid; after ¼ hr. the hydrolysate gave a series of ninhydrin-positive spots on a paper chromatogram. The two of these with the highest R_F values were identified as glutamic acid and γ-glutamylglutamic acid; the other spots were assigned to higher members of the homologous series of peptides, such as are formed by the action of hydrobromic acid on poly-L-lysine (Waley and Watson, *Biochem. J.*, 1953, **55**, 328). This assignment is supported by the linear plot of $\ln[(1/R_F) - 1]$ against the assumed number of glutamic acid residues in the peptide (Pardee, *J. Biol. Chem.*, 1951, **190**, 757; Waley and Watson, *J.*, 1953, 475); the values of the constants A and B in Pardee's equation were −510 cal./mole and −100 cal./mole respectively. Similar results were obtained on partial hydrolysis of the synthetic γ-linked polypeptide; it can be concluded from these results, and from the infrared spectra, that there is no evidence for any α-glutamyl linkages in the naturally occurring poly-D-glutamic acids.

The γ-linked polypeptide also resembled the natural products (and differed from the synthetic α-linked polypeptide) in its ready solubility in water and the value of its ionisation constant. In the titration of a weak acid with a strong base, the value of the ionisation constant (K) at any stage of the titration is accurately given by

$$K = [H^+](b + [H^+] - [OH^-])/(a - b - [H^+] + [OH^-])$$

where b is the concentration of added base, and a the total concentration of acid; in the pH region (2·5 − 5) with which we are concerned, the term $[OH^-]$ may be neglected, giving

$$K = [H^+](b + [H^+])/[a - b - [H^+]) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The titrations of these polypeptides were carried out in N-potassium chloride, so as to minimise the interaction between the charged groups; if there is no such interaction, the titration curve of a polymeric acid may be represented by one titration constant (Simms, *J. Amer. Chem. Soc.*, 1926, **48**, 1239; von Muralt, *ibid.*, 1930, **52**, 3518). The value of K [found by means of equation (1)] decreased, however, with increasing degree of ionisation, showing that even at this ionic strength interaction occurs. The value of pK of the synthetic γ-linked and natural polyglutamic acids was 3·6 ± 0·1 at 50% ionisation, in N-potassium chloride at 25°.

The positive ninhydrin reaction given by γ-linked peptides of glutamic acid has been mentioned. It was found that a 0·25% solution of sodium poly-D-glutamate approximately matched a 0·005% solution of glutamic acid in the intensity of colour produced on heating with ninhydrin in acetate buffer: if the only groups reacting were the terminal amino-groups of the polymer, its degree of polymerisation would be about 50. In fact, the degree of polymerisation of this sample was of the order of a thousand, so that much of the amide-nitrogen must enter into the reaction with ninhydrin, which thus resembles the reaction with nitrous acid.

The molecular weights of these polypeptides were measured by arylation of their amino-groups with 1-fluoro-2 : 4-dinitrobenzene, with a slight modification of Levy's method (*Nature*, 1954, **174**, 126), followed by hydrolysis with perchloric acid in formic acid (Hanes, Hird, and Isherwood, *Biochem. J.*, 1952, **51**, 25); the amount of 2 : 4-dinitrophenylglutamic acid thus liberated was compared with the amount obtained after reaction of the glutamic acid with 1-fluoro-2 : 4-dinitrobenzene. The molecular weight of the synthetic polypeptide was about 9000; that of the polypeptide from *B. licheniformis* about 90,000, and of that from *B. anthracis* of the order of 100,000 [Dr. L. H. Kent found a value of 180,000 for the polypeptide from *B. anthracis* (personal communication)]. During this work, *N*-2 : 4-dinitrophenylglutamic acid was obtained crystalline for the first time.

Apparently poly-D-glutamic acid from *B. anthracis* has one of the longest peptide chains known; it is found both inside and outside the cells of *B. anthracis* grown *in vivo* (Smith and Zwartouv, *Biochem. J.*, 1954, **56**, viii; Smith, Zwartouv and Gallop, *ibid.*, p. ix), and is concentrated in the capsules surrounding the cells. It has been reported (Ivanovics and St. Horváth, *Acta Physiol. Sci. Hung.*, 1953, **4**, 401) that the carboxyl groups of the polypeptide in the capsules are not free, and the polypeptide may play an important part in the spatial organisation of the capsule.

Experimental

Benzyloxycarbonyl-γ-L-glutamylhydrazide.—Hydrogen chloride was passed into a cooled suspension of L-glutamic acid (125 g.) in methanol (2500 ml.). After 4½ hr., the solution was neutralised with aqueous ammonia (*d* 0·88; 65 ml.) and kept in the refrigerator overnight. γ-Methyl L-glutamate (99 g.) was collected, and acylated by stirring it with water (700 ml.) containing potassium hydrogen carbonate (137 g.) and benzyl chloroformate (120 ml.) at room temperature for 6 hr. The solution was extracted with ether and then acidified: the γ-methyl benzyloxycarbonyl L-glutamate was isolated with ethyl acetate [the ethyl acetate solution being washed with water containing potassium hydrogen carbonate (5 g.)], dissolved in ethanol (250 ml.), and treated with 90% hydrazine hydrate (100 ml.). After 48 hr., the benzyloxycarbonyl-γ-L-glutamylhydrazide was isolated as described by Le Quesne and Young (*J.*, 1950, 1959): the yield was 120 g. (48% overall from glutamic acid), and the m. p. 173—174° (pure enough for the next stage).

γ-Benzyl N-(Benzyloxycarbonyl-γ-L-glutamyl)-L-glutamate.—Sodium nitrite (10·7 g.) in water (107 ml.) was added during 12 min. to a cooled, stirred solution of benzyloxycarbonyl-γ-L-glutamylhydrazide (32 g.) in water (256 ml.) containing 6N-hydrochloric acid (109 ml.) covered with ether (528 ml.). After separation, the aqueous layer was extracted with cooled ether, and the combined ethereal layers were washed thrice with cooled water and promptly added to γ-benzyl L-glutamate (25 g.) (Hanby, Waley, and Watson, *J.*, 1950, 3239; average yield 30%) and potassium hydrogen carbonate (32 g.) in water (320 ml.). The mixture was stirred at room temperature for 6 hr. The next day, the filtered solution was covered with ethyl acetate and acidified (caution: hydrazoic acid evolved). The ethyl acetate extracts were washed, dried, concentrated to 120 ml., and diluted with ether (220 ml.); *γ-benzyl (benzyloxycarbonyl-γ-L-glutamyl)-L-glutamate* (31·6 g., 58%; m. p. 154—156°) separated. Recrystallisation by dissolution in acetone–ethyl acetate, concentration, and dilution with ether raised the m. p. to 159·5—160°, $[\alpha]_D^{21}$ +11·5° (*c*, 1·92 in acetic acid) (Found: C, 59·7; H, 5·9; N, 5·8. $C_{25}H_{28}O_9N_2$ requires C, 60·0; H, 5·6; N, 5·6%).

γ-Benzyl α-Methyl N-(α-Methylbenzyloxycarbonyl-γ-L-glutamyl)-L-glutamate.—Excess of ethereal diazomethane was added to γ-benzyl (benzyloxycarbonyl-γ-L-glutamyl)-L-glutamate (17 g.) in methanol (300 ml.), and the solvents were removed. The residual *γ-benzyl α-methyl (α-methylbenzyloxycarbonyl-γ-L-glutamyl)-L-glutamate* (12·6 g., 70%), recrystallised from ethyl

acetate–light petroleum (b. p. 80—100°), had m. p. 117—118°, $[\alpha]_D^{21}$ +6° (*c*, 1·88 in acetic acid) (Found: C, 61·7; H, 5·8; N, 5·15. $C_{27}H_{32}O_9N_2$ requires C, 51·4; H, 6·1; N, 5·3%).

α-Methyl N-(*α-Methyl-γ-*L-*glutamyl*)-L-*glutamate*.—*γ*-Benzyl α-methyl (α-methylbenzyloxycarbonyl-*γ*-L-glutamyl)-L-glutamate (12·6 g.) in methanol (270 ml.), acetic acid (10 ml.), and water (20 ml.) was reduced in hydrogen in the presence of palladium black (2 g.) for 2½ hr. The filtered mixture was evaporated, and the residue recrystallised from 95% *iso*propanol; *α-methyl* N-(*α-methyl-γ-*L-*glutamyl*)-L-*glutamate* (5·4 g., 70%) had m. p. 123—124°, $[\alpha]_D^{21}$ +23° (*c*, 2·03 in acetic acid) (Found: C, 44·6; H, 6·95; N, 9·15. $C_{12}H_{20}O_7N_2,H_2O$ requires C, 44·7; H, 6·8; N, 8·7. Found, on material dried at 100°: C, 48·0; H, 6·5. $C_{12}H_{20}O_7N_2$ requires C, 47·3; H, 6·6%).

*Poly-(γ-*L-*glutamyl)-*L-*glutamic Acid*.—α-Methyl *N*-(α-methyl-*γ*-L-glutamyl)-L-glutamate hydrate (0·6 g.), diethyl phosphite (2·8 ml.), and tetraethyl pyrophosphite (1·6 ml.) were heated at 100° for 10 min., the solvent was distilled off, and the residue was triturated under ether. The sticky polymethyl ester was hydrolysed with N-sodium hydroxide (8 ml.) for 10 min., and the solution then dialysed against running tap-water for 40 hr. and finally against distilled water for 4 hr. Freeze-drying gave *sodium poly-(γ-*L-*glutamyl)-*L-*glutamate* (0·12 g., 31%) as a dihydrate, which, however, still contained phosphorus [Found: C, 32·4; H, 5·6; N, 7·6; P, 1·8; degree of polymerisation (see below), 55. $(C_9H_6O_9NNa)_n,2H_2O$ requires C, 32·1; H, 5·35; N, 7·5%). For further purification, the aqueous solution of this salt was treated with aqueous copper sulphate, the precipitated copper salt was washed thoroughly and dissolved in 0·25N-hydrochloric acid, and the solution was dialysed against 0·005N-hydrochloric acid for 24 hr.; freeze-drying gave *poly-(γ-*L-*glutamyl)-*L-*glutamic acid* (Found: C, 40·9; H, 5·9; N, 9·55; P, 0·6. $C_5H_7O_3N,H_2O$ requires C, 40·8; H, 6·1; N, 9·5%).

*γ-*L-*Glutamyl-*L-*glutamic Acid*.—*γ*-Benzyl (benzyloxycarbonyl-*γ*-L-glutamyl)-L-glutamate was hydrogenated in aqueous acetic acid, and *γ*-L-glutamyl-L-glutamic acid isolated as described by Le Quesne and Young (*loc. cit.*); it had $[\alpha]_D^{20}$ +3·4° (*c*, 1·0 in 0·5N-hydrochloric acid), and on hydrolysis furnished optically pure L-glutamic acid (Sachs and Brand, *J. Amer. Chem. Soc.*, 1953, **75**, 4608, give $[\alpha]_D^{24}$ +3·8° in 0·5N-hydrochloric acid); paper chromatography showed it to be free from the α-dipeptide.

*Isolation of Poly-*D-*glutamic acid from* B. licheniformis.—The organism was kindly supplied by Dr. Bovarnick, and was grown as described by Bovarnick, Eisenberg, O'Connell, Victor, and Owades (*J. Biol. Chem.*, 1954, **207**, 593); the copper salt was precipitated from the medium (600 ml.), washed with water acidified to pH 3, and decomposed with 0·5N-hydrochloric acid (10 ml.). The filtered solution was dialysed against 0·005N-hydrochloric acid at 2° for 70 hr., filtered again, and freeze-dried, giving 74 mg. of a colourless solid (Found: C, 41·7; H, 5·75; N, 9·25. Calc. for $C_5H_7O_3N,H_2O$: C, 40·8; H, 6·1; N, 9·5%).

Partial Hydrolysis of Polyglutamic Acid.—Sodium poly-D-glutamate (10 mg.) in constant-boiling hydrobromic acid (0·1 ml.) was kept at 100°; samples (0·02 ml.) were periodically withdrawn and added to 50% pyridine (0·2 ml.), and this solution analysed by paper chromatography, using as solvent *n*-butanol–acetic acid–water–pyridine (30 : 6 : 24 : 20). The relative intensities (evaluated visually) of the spots are shown in the Table below.

Of the products, glutamic acid and *γ*-glutamylglutamic acid were identified by comparison with authentic samples; the assignment of the higher peptides has already been discussed. There were no ninhydrin-positive spots at the beginning of the reaction with either specimen of poly-D-glutamic acid; the synthetic polypeptide, however, showed some spots near the starting line which disappeared during the course of the reaction; this difference may be attributed to the higher molecular weights of the natural polypeptides.

Product	Time of hydrolysis (hr.). 0·25	0·5	0·75	1·25
Glutamic acid	+	++	+++	++++
γ-Glutamylglutamic acid	++	++	+	±
Assumed tripeptide	+	+	±	—
Assumed tetrapeptide	+	±	—	—
Assumed pentapeptide	+	—	—	—
Assumed hexapeptide	+	—	—	—

End-group Estimation.—Sodium poly-(*γ*-L-glutamyl)-L-glutamate (7 mg.) in 0·025M-borax (0·2 ml.) and 1-fluoro-2 : 4-dinitrobenzene (1 mg.) were stirred at 40° in the dark for 80 min. The cooled solution was extracted with ether, acidified, extracted with ether again, dialysed against distilled water for 6 hr., and evaporated to dryness *in vacuo*. The residue was transferred with a 10% solution of 60% perchloric acid in 98% formic acid (0·3 ml.) to a test-tube, the end

of which was then drawn out into a capillary (as considerable pressure is generated in the subsequent heating). After being kept for 4 hr. at 100° in the dark, the solution was diluted with water (3 ml.) and extracted thrice with ether (solution A). The aqueous solution was extracted thrice with water-saturated ethyl methyl ketone (to remove formic acid) and once with ether. The combined ethyl methyl ketone extracts were washed with a little water, which was added to the aqueous solution. This was then brought to pH 9 with N-sodium hydroxide (0·6 ml.), borax (90 mg.) and 1-fluoro-2 : 4-dinitrobenzene (16 mg.) added, and the mixture stirred at 40° in the dark for 80 min. The cooled solution was extracted with ether, acidified, and extracted thrice with ether, and this ethereal solution (B) diluted to a volume of 20 ml. One-third of solution A and 0·5 ml. of solution B were run on a paper chromatogram, using as solvent 1·5M-phosphate buffer (pH 6), and the amounts of dinitrophenylglutamic acid were estimated as described by Levy (*Nature*, **1954**, **174**, 126); after correction for the paper blanks, the optical density of the solution corresponding to solution A was 0·175, and of that corresponding to solution B, 0·71. Hence the number-average degree of polymerisation was 55. The end-group estimation on other polymers was carried out in the same way.

N-(2 : 4-*Dinitrophenyl*)-L-*glutamic Acid*.—L-Glutamic acid (209 mg.) was treated with 1-fluoro-2 : 4-dinitrobenzene (350 mg.) as described by Levy (*loc. cit.*). The crude product was washed first with benzene, and then with ether–benzene (1 : 19), giving crystalline 2 : 4-dinitrophenyl-L-glutamic acid (248 mg., 58%), m. p. 93·5—94·5° (Found: C, 41·9; H, 3·7; N, 13·3. Calc. for $C_{11}H_{11}O_8N_3$: C, 42·2; H, 3·5; N, 13·4%).

I thank Sir Robert Robinson, O.M., F.R.S., for his advice and encouragement; Dr. L. H. Kent (Ministry of Supply, Porton) for poly-D-glutamic acid from *B. anthracis*; Dr. M. Bovarnick (State University of New York) for the strain of *B. licheniformis* used; and Dr. J. Watson (Courtaulds Ltd., Maidenhead) for carrying out the potentiometric titrations. This work was carried out during the tenure of a Pressed Steel Co. Ltd. Research Fellowship.

The Dyson Perrins Laboratory, University of Oxford. [*Received, October 23rd*, 1954.]

A Method of reducing Phenols to Aromatic Hydrocarbons.

By G. W. Kenner and N. R. Williams.

[Reprint Order No. 5839.]

Simple phenols are easily converted by means of diethyl phosphorochloridate or tetraethyl pyrophosphate into aryl diethyl phosphates. The aromatic hydrocarbons corresponding to the phenols are the principal products of reaction between these esters and solutions of sodium or lithium in liquid ammonia. The reaction is much less successful with dihydric phenols.

It was shown by Sowa and his co-workers (*J. Amer. Chem. Soc.*, 1937, **59**, 603, 1488; 1938, **60**, 94) that diaryl ethers react with a solution of sodium in liquid ammonia according to the equation $ArOAr' + 2Na + NH_3 = ArH + Na{\cdot}NH_2 + NaOAr'$. An analogous reaction might take place with an aryl ester of any oxy-acid, provided that the acyl residue is not easily attacked by the sodium solution. We have been led to investigate this possibility by the notion that a generally successful reaction, coupled with an esterification step, would provide another method of reducing phenols to aromatic hydrocarbons. The aryl toluene-*p*-sulphonates were the obvious choice, but they are very sparingly soluble in liquid ammonia. We found that the methanesulphonyl derivatives of *p*-phenylphenol and α-naphthol are likewise insoluble, but that *m*-acetamidophenyl and *p*-methoxyphenyl methanesulphonate are both moderately soluble in liquid ammonia and are reduced by sodium in about 40% yield to acetanilide and anisole, respectively. In contrast with the sulphonic esters, all the aryl diethyl phosphates which we have examined are freely soluble in liquid ammonia. In many cases their reduction takes the expected course; it has already been recorded that sodium phosphate is produced from diphenyl hydrogen phosphate by reaction with sodium in liquid ammonia (Baddiley and Thain, *J.*, 1953, 1610).

The aryl esters of diethyl phosphoric acid were prepared from both the acid chloride and the acid anhydride. The most convenient method was to add the calculated quantity of triethylamine to a carbon tetrachloride solution of the phenol and diethyl phosphite, made directly from ethanol and phosphorus trichloride (McCombie, Saunders, and Stacey, *J.*, 1945, 380). Diethyl phosphorochloridate was produced by base-catalysed reaction between the phosphite and carbon tetrachloride (Atherton, Openshaw, and Todd, *J.*, 1945, 660; Atherton and Todd, *J.*, 1947, 674; Steinberg, *J. Org. Chem.*, 1950, **15**, 637) and the over-all reaction was :

$$ArOH + HO{\cdot}P(OEt)_2 + CCl_4 + NEt_3 = ArO{\cdot}P(O)(OEt)_2 + CHCl_3 + NHEt_3Cl$$

Alternatively, an aqueous solution of the sodium phenoxide was treated with the water-soluble anhydride, tetraethyl pyrophosphate, which is commercially available. A slight disadvantage of this procedure was that the precipitated ester extracted some of the anhydride from the aqueous phase. All the esters of monohydric phenols prepared so far have been viscous oils showing no tendency to crystallise.

All the aryl diethyl phosphates listed in Table 1 were reduced easily when either lithium or sodium was added to their solutions in liquid ammonia. The amount of metal required according to the following equation was consumed before the blue colour appeared :

$$ArO{\cdot}P(O)(OEt)_2 + 2M + NH_3 = ArH + M{\cdot}NH_2 + MO{\cdot}P(O)(OEt)_2$$

At the end of the reaction it was convenient to add alcohol before isolating the products. The presence of alcohol during the reduction, or the use of excess of metal, gave poor results, presumably owing to reduction of the aromatic nucleus (Birch, *Quart. Rev.*, 1950, **4**, 69). The yields of hydrocarbon (Table 2) varied around 75% and therefore the above equation does not account for the whole of the reaction. The minor products were the phenol and a bicarbonate-soluble oil, possibly the aryl ethyl hydrogen phosphate. These substances could have arisen from attack by the metal on the phosphoryl groups. This may have been the major course of reaction in the cases of *o*- and *p*-chlorophenyl diethyl phosphates, or ammonolysis may have competed with the sluggish reduction; considerable quantities of the chlorophenols were produced by reaction with either sodium or lithium. The latter did not dissolve smoothly in the usual way. Gilman, Zoellner, and Selby (*J. Amer. Chem. Soc.*, 1933, **55**, 1252) have recorded failure to metalate *p*-dibromobenzene and *p*-bromochlorobenzene with lithium, although good yields were obtained with other aryl bromides. The diethyl phosphate of methyl salicylate gave about 20% of methyl benzoate despite the obvious side-reactions of the methoxycarbonyl group.

The success of these experiments with monohydric phenols encouraged the hope that it would be possible to use the reaction as a stage in the reduction of quinones to aromatic hydrocarbons. However, benzene could not be detected as a product of the reaction between the bis(diethyl phosphoryl) derivative of quinol and 4 equivs. of lithium. Nor did reaction with 2 equivs. of lithium appear to give diethyl phenyl phosphate, which can itself be reduced in good yield to benzene. On the other hand, the derivatives of resorcinol and catechol gave modest yields of benzene (30% and 15% respectively) on reduction with either lithium or sodium. Similarly in the naphthalene series, no naphthalene could be obtained from the esters of 1 : 4- and 1 : 5-dihydroxynaphthalene, but about 20% was produced from the 1 : 6-, 2 : 6-, and 2 : 7-isomers. In all these cases the product was mainly a mixture of alkali-soluble oil and neutral oil of high boiling point. Thus the method seems to have little practical value for dihydric phenols, but the nature of the reaction with the quinol derivative deserves further investigation.

Another way of reducing phenols to aromatic hydrocarbons (Kenner and Murray, *J.*, 1949, S 178) consists in hydrogenating the toluene-*p*-sulphonates in presence of Raney nickel. When the two methods are equally effective the new one is more convenient. Hydrogenolysis of the phosphate esters of *m*-acetamidophenol and 3 : 5-xylenol was unsuccessfully attempted with a sample of Raney nickel which catalysed the toluene-*p*-sulphonate reduction. Some 10% of reduction was detected when platinised nickel (Levering, Morritz, and Lieber, *J. Amer. Chem. Soc.*, 1950, **72**, 1190) was used, but this

was not consistently reproducible. Hydrogenation with Adams platinum catalyst has often been used for the removal of phenyl groups from phosphates (Brigl and Müller, *Ber.*, 1939, **72**, 2121) and it produced *N-cyclo*hexylacetamide from *m*-acetamidophenyl diethyl phosphate. Interruption of the reaction when only one mol. of hydrogen had been absorbed yielded, not acetanilide, but a mixture of the hexahydro-compound and unchanged ester. We therefore believe that saturation of the aromatic ring is essential for the platinum-catalysed cleavage of the carbon–oxygen link and is not merely a subsequent process as originally postulated by Brigl and Müller (*loc. cit.*). This is reasonably explained by the assumption that it is the intermediate allyl-type phosphates which suffer hydrogenolysis.

Experimental

Preparation of Aryl Diethyl Phosphates.—(a) *From diethyl phosphite.* Triethylamine (14·3 c.c., 0·104 mole) was added slowly with vigorous shaking to an ice-cooled solution of the phenol (0·1 mole) in carbon tetrachloride (30 c.c.) and diethyl phosphite (13·4 c.c., 0·104 mole; McCombie, Saunders, and Stacey, *J.*, 1945, 380). Towards the end of the addition triethylamine hydrochloride began to separate as white needles and eventually a solid mass was formed. This was kept overnight at room temperature and then diluted with water. The organic layer was washed once with dilute hydrochloric acid, four times with dilute sodium hydroxide solution, and once with water before being dried (K_2CO_3) and evaporated under reduced pressure. The residual yellow-brown syrup, obtained in the yield recorded in Table 1, was pure enough for use in reductions, but was distilled in a tube at 120°/10^{-3} mm. before analysis.

(b) *From tetraethyl pyrophosphate.* Tetraethyl pyrophosphate (25·4 c.c., 0·104 mole; supplied by Albright and Wilson Ltd.) was added in one portion to a solution of the phenol (0·1 mole) in N-sodium hydroxide (104 c.c.). The mixture was vigorously shaken and became opaque in 15—30 sec. The brown oil which separated was extracted into ethyl acetate (50 c.c.) and washed with N-sodium hydroxide (4 × 50 c.c.) and then water. Evaporation of the dried (K_2CO_3) ethyl acetate left the tabulated yield of red-brown oil.

Table 1. *Aryl diethyl phosphates*, $ArO{\cdot}P(O)(OEt)_2$.

No.	Ar	Yield from (a)	Yield from (b)	n_D^{25}	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
1	Ph	95	—	1·475	$C_{10}H_{15}O_4P$	51·9	6·8	52·2	6·5
2	*p*-Me·C_6H_4	94	—	1·473	$C_{11}H_{17}O_4P$	54·0	7·0	54·1	7·0
3	*m*-Me·C_6H_4	96	—	1·472	$C_{11}H_{17}O_4P$	53·9	6·9	54·1	7·0
4	*o*-Me·C_6H_4	83	—	1·476	$C_{11}H_{17}O_4P$	54·2	7·1	54·1	7·0
5	*p*-MeO·C_6H_4	98	—	1·487	$C_{11}H_{17}O_5P$	51·0	6·5	50·7	6·6
6	*m*-MeO·C_6H_4	78	—	1·484	$C_{11}H_{17}O_5P$	51·0	6·9	50·7	6·6
7	*o*-MeO·C_6H_4	85	—	1·486	$C_{11}H_{17}O_5P$	50·6	7·1	50·7	6·6
8	*p*-NHAc·C_6H_4	89	—	1·510	$C_{12}H_{18}O_5NP$	50·0	6·5	50·1	6·3
9	*m*-NHAc·C_6H_4	—	91	1·509	$C_{12}H_{18}O_5NP$	49·9	6·4	50·1	6·3
10	*p*-$C_6H_5{\cdot}C_6H_4$	87	—	1·548	$C_{16}H_{19}O_4P$	63·0	6·4	62·7	6·3
11	3 : 5-$C_6H_3Me_2$	—	84	1·480	$C_{12}H_{19}O_4P$	56·0	7·6	55·8	7·4
12	α-$C_{10}H_7$	—	91	1·547	$C_{14}H_{17}O_4P$	60·3	6·1	60·0	6·1
13	β-$C_{10}H_7$	97	73	1·544	$C_{14}H_{17}O_4P$	60·3	6·2	60·0	6·1

Reduction of Aryl Diethyl Phosphates.—The ester (about 15 g.) was dissolved in liquid ammonia (about 150 c.c., direct from a cylinder) in a 500-c.c. conical flask; no precautions were taken to exclude moisture. The metal (exactly 2 atomic proportions) was added in small pieces during about 5 min. (as fast as frothing would allow) to the solution, which was shaken by hand. In cases in which the solution was not too dark the blue colour then became persistent. Alcohol (2 mols.) was added and the ammonia allowed to evaporate while the flask was left for several hours. The product was taken up in ether (50 c.c.), washed with sodium hydrogen carbonate solution and sodium hydroxide solution, and recovered by evaporation. The tabulated yields refer to this material, which was found by subsequent distillation or recrystallisation to be of good quality. A series of experiments with esters 9 and 11 showed that the yield was unaffected by the following variations: dissolution of the ester in ether (25 c.c.) before addition of the ammonia, addition of a solution of the metal in ammonia, addition of a solution of the ester in ammonia to a solution of the metal in ammonia, omission of the final addition of ethanol. A less pure sample of acetanilide was obtained from ester No. 9 when ammonium chloride was added instead of ethanol.

TABLE 2. *Reduction of aryl diethyl phosphates.*

Ester no.	1	2	3	4	5	6	7	8	9	10	11	12	13
Yield on using Li	82[a]	75[b]	54[b]	63[b]	85	—	88	60	93	75	63	71	88
Yield on using Na	—	—	—	—	88	85	90	76	89	80	58	57	95

[a] Estimated from the intensity of ultra-violet absorption curve, identical in shape with that of pure benzene, after allowance for a loss of 45% during evaporation of the ammonia. [b] Toluene estimated in the same way as the benzene, with allowance for a loss of 25%.

Preparation of Aryl Methanesulphonates.—Methanesulphonyl chloride (1·1 mols.) was added to a solution of the phenol in a slight excess of N-sodium hydroxide. The mixture was immediately shaken vigorously in order to prevent coagulation of the chloride with the ester, which soon crystallised. The ester was collected and recrystallised from water or aqueous alcohol. m-*Acetamidophenyl methanesulphonate* (yield 78%), m. p. 107·5—108° (Found: C, 46·9; H, 4·7. $C_9H_{11}O_4NS$ requires C, 47·1; H, 4·8%), and p-*methoxyphenyl methanesulphonate* (yield 40%), m. p. 79·5—80° (Found: C, 47·2; H, 5·1. $C_8H_{10}O_4S$ requires C, 47·5; H, 5·0%), were reduced, as described above for the phosphates, by sodium in liquid ammonia to acetanilide (40%) and anisole (38%) respectively.

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, November 2nd*, 1954.]

The Structure of Cyperone. Part II. The Alkali-catalysed Isomerisation of α-Cyperone and an Autoxidation.*

By H. M. E. CARDWELL and F. J. MCQUILLIN.

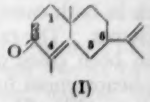
[Reprint Order No. 5526.]

The action of alcoholic alkali on α-cyperone (I), reported to lead to an isomeric ketone, is chiefly to induce autoxidation to the 6-hydroxy-derivative (V) though it may in small part be associated with the presence in natural cyperone of an *iso*propylidene isomer (III).

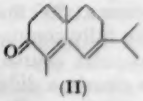
α-CYPERONE has been shown to have the structure (I) (Bradfield, Pritchard, and Simonsen, *J.*, 1937, 763; Bradfield, Hegde, Rao, Simonsen, and Gillam, *J.*, 1936, 667). An isomeric ketone obtained from it by acid digestion (Bradfield, Hegde, *et al.*, *loc. cit.*), and regarded on the basis of oxidation experiments as a diastereoisomer arising by inversion at $C_{(6)}$, was later shown (Part I) to consist of a mixture of α-(I) and the structurally isomeric β-cyperone (II).

Acid-catalysed isomerisation of (I) to (II) has well-known analogies and the mechanism is clear. Bradfield, Hegde, *et al.*, however, refer without experimental details to obtaining the isomerised ketone also by alkali digestion of α-cyperone.

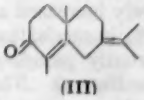
Simonsen and Barton ("The Terpenes," Vol. III, Cambridge Univ. Press, 1952, p. 209) state this was by means of methyl-alcoholic potassium hydroxide. Since alkali should not readily induce isomerisation of (I) and the product reported appeared to be only partially isomerised, we were inclined to infer the presence in α-cyperone of some of the *iso*propylidene isomer (III), which would be expected to pass readily by enolisation into (II) under acid or alkaline conditions.



(I)



(II)



(III)

Evidence was sought in the intensity of absorption at *ca.* 890 cm.$^{-1}$ (*ca.* 11·28 μ) of α-cyperone in comparison with a synthetic specimen (cf. Adamson, McQuillin, Robinson,

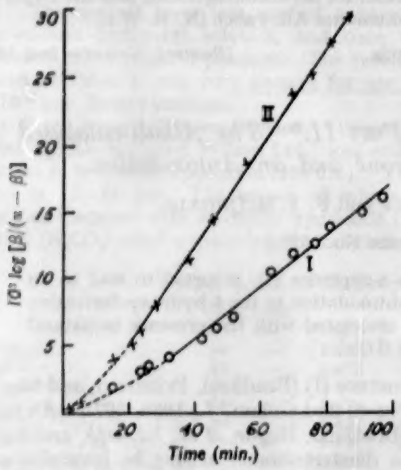
* The paper, *J.*, 1951, 716, is regarded as Part I.

and Simonsen, *J.*, 1937, 1576; and the following paper), and with related compounds. Barnard, Bateman, Harding, Koch, Sheppard, and Sutherland (*J.*, 1950, 915) have indicated that absorption in this region is a sensitive index of the *iso*propenyl group in simpler terpenes. The results (see Table) indicated apparently reduced absorption due to terminal methylene in natural α-cyperone. Its oxime, however, gave a high extinction value in

ε (*l. mole*$^{-1}$ *cm.*$^{-1}$) *at* ~11·28 μ *in carbon disulphide.*

	ε	λ (μ)		ε	λ (μ)
α-Cyperone, natural	121	11·26	" β-Cyperone " oxime, natural	100	11·28
,, synth.	170	11·25	β-Cyperone oxime, synth.	0	—
,, oxime, natural	207	11·28	(−)-Dihydrocarvoxime	176	11·27
,, ,, synth.	171	11·28			

contrast with the consistent group formed by the synthetic and related oximes, " β-cyperone " oxime from natural sources being known from its ultraviolet absorption to be a mixture of (I) and (II) (Part I). The extinction coefficient of *ca.* 170 shown by a number of these substances is in good agreement with the value of 155—160 found by Barnard *et al.* (*loc. cit.*) for substances known to exist in the *iso*propenyl form. These



Rate of apparent isomerisation of natural (I) and synthetic α-cyperone (II) in n-alcoholic potassium hydroxide.

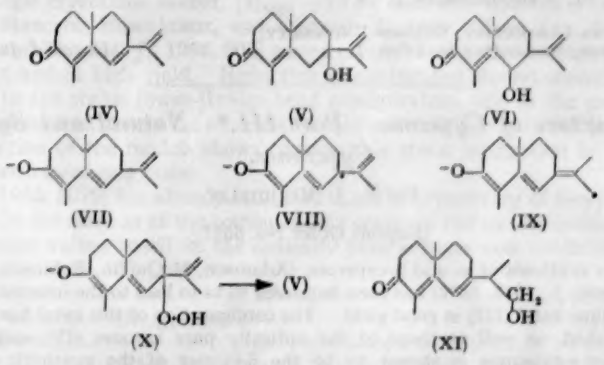
authors moreover also encountered anomalously high absorption in some cases; reduced absorption is, however, probably more significant. The low ε value for the natural ketone may therefore indicate the presence of some of (III) in the natural ketone but the high absorption shown by the oxime renders this conclusion tentative.

The amount of natural α-cyperone available did not permit close investigation; the small remaining sample was kindly made available by Dr. L. N. Owen and Sir John Simonsen to whom our best thanks are offered. After digestion with hot alcoholic potassium hydroxide this showed increased absorption at 300 mμ, corresponding to the presence of only 3—4% of the conjugated isomer (II): the main absorption at 250 mμ remained essentially unchanged.

In alcoholic alkali at the room temperature, the natural and the synthetic ketone showed progressively increased absorption at 300 mμ which in both cases came to an end at an apparent 20% isomerisation to the fully conjugated isomer. The rate of this change followed an apparently pseudo-unimolecular course but in both cases only after an induction period (see Figure). This was clearly a different phenomenom from the isomerisation, and its kinetics suggested an oxidation. Treibs (*Ber.*, 1931, **64**, 2178, 2545, and later papers) has recorded a number of examples of autoxidation of αβ-unsaturated ketones under alkaline conditions. Indeed, the synthetic ketone (I), after being kept for some days in alcoholic potassium hydroxide at room temperature, was converted into a crystalline

hydroxy-ketone $C_{15}H_{22}O_2$ in good yield. This showed infrared absorption bands at 2·85 (OH), 11·28 (terminal CH_2:), and 6·05 μ (C:C·CO; confirmed by ultra-violet absorption at 250 mμ, log ε 3·91). On hydrogenation two mols. of hydrogen were absorbed. With acetic anhydride the substance was not dehydrated but gave a liquid acetate. With 2 : 4-dinitrophenylhydrazine, however, in strongly acid solution the elements of water were lost to give a derivative having $\lambda_{max.}$ 420 mμ (log ε 4·58 in $CHCl_3$), which clearly corresponds with the trienone (IV); the 2 : 4-dinitrophenylhydrazone of the dienone (II) gave $\lambda_{max.}$ 404 mμ (log ε 4·57), and that of the monounsaturated ketone (I) gave $\lambda_{max.}$ 386 mμ (log ε 4·39) (in EtOH) (Part I). The wave-length increments are comparable. These results indicate structure (V) or (VI) for the hydroxy-ketone. Neither structure is in complete accord with recovery of the substance unchanged after refluxing with aqueous-alcoholic alkali; under these conditions a hydroxy-ketone (V) should be dehydrated, and (VI) isomerised to the 3 : 5-diketone (cf. Heilbron, Jones, and Spring, *J.*, 1937, 801; Ellis and Petrov, *J.*, 1939, 1078). Structure (V) is preferred since the substance was not oxidised by manganese dioxide, a reagent known to oxidise αβ-unsaturated primary or secondary alcohols (cf. Attenburrow *et al.*, *J.*, 1952, 1094; Amendolla, Rosenkranz, and Sondheimer, *J.*, 1954, 1226).

The oxidation therefore appears to follow a somewhat different course from the examples discussed by Treibs (*loc. cit.*). It seems most reasonable to associate oxidation at $C_{(6)}$ with the analogy between the enolic form (VII) present in strongly alkaline solution and the environmentally analogous methylene present in the autoxidisable dienoic acids. The intermediate hydroperoxides are known to be decomposed in alkaline solution to the corresponding hydroxy-derivative (cf. Hock and Gänicke, *Ber.*, 1938, **71**, 1430; Farmer and Sundralingam, *J.*, 1942, 121), leading *via* (X) to (V).



The formation of the intermediate radical (VIII) may clearly have a bearing on the alkali-catalysed isomerisation discussed above since the mesomeric form (IX) may lead to (XI), a hydroxy-derivative of the conjugated ketone (II). This interpretation and the generality of the autoxidation reaction in other cases are being examined. The development of conjugation during autoxidation of some unconjugated dienes is, however, already well-known (cf., *e.g.*, Farmer, Koch, and Sutton, *J.*, 1943, 541).

Experimental

$[\alpha]_D$ are for solutions in $CHCl_3$. Infrared measurements were carried out by Dr. F. B. Strauss, The Dyson Perrins Laboratory, Oxford, whom we thank. The specimens employed were (i) α-cyperone, natural, kindly made available by Dr. L. N. Owen, Imperial College of Science, London, whom we thank, (ii) the oxime of natural α-cyperone, a specimen provided by Sir John Simonsen, (iii) synthetic α-cyperone, $[\alpha]_{5461}$ +210°, and its oxime, prepared by the improved method described in the following paper, (iv) "natural" and synthetic β-cyperone oximes, previously reported (Adamson, McQuillin, Robinson, and Simonsen, *loc. cit.*). The

natural ketone had undergone some oxidation and for characterisation a small sample was purified by chromatography on alumina. Elution by light petroleum gave the ketone as a colourless oil, b. p. 85°/0·05 mm., n_D^{17} 1·5292, $[\alpha]_{5461}$ +119·2° (*c* 1·03), $\lambda_{max.}$ 250 mμ (log ε 4·17), λ 300 mμ log ε 1·55) (Found: C, 82·7; H, 10·4. Calc. for $C_{15}H_{22}O$: C, 82·6; H, 10·1%).

Alkali-induced Isomerisation.—α-Cyperone (natural) (0·1 g., not purified by chromatography) was heated with 10% alcoholic potassium hydroxide (2·5 c.c.) on the steam-bath for 4 hr. Recovered by dilution with water (without acidification) the ketone afforded a colourless oil, b. p. 95°/0·1 mm., n_D^{20} 1·5313, $[\alpha]_{5461}$ +129·5° (*c* 0·29), $\lambda_{max.}$ 251 mμ (log ε 4·11), λ 300 mμ (log ε 3·007).

Autoxidation of Synthetic α-Cyperone.—Synthetic α-cyperone (1·5 g.) in alcohol (20 c.c.) was treated with potassium hydroxide (1·5 g.) in water (7 c.c.) and kept loosely corked at room temperature for 9 days. The material recovered by dilution gave on distillation a viscous colourless oil (1·1 g.), b. p. 115—120°/0·1 mm., n_D^{18} 1·5418, which solidified, to give 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*octahydro*-6-*hydroxy*-4 : 9-*dimethyl*-3-*oxo*-6-iso*propenylnaphthalene*, m. p. 61°, as prisms from light petroleum, $[\alpha]_{5461}$ +100° (*c*, 1·0), $\lambda_{max.}$ 250 mμ (log ε 3·92) (Found: C, 76·7; H, 9·4. $C_{18}H_{28}O_3$ requires C, 77·0; H, 9·4%). Refluxing for some hours with acetic anhydride and distillation gave an *acetate*, b. p. 100—105°/0·05 mm., n_D^{17} 1·5210 (Found: C, 74·3; H, 9·1. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·7%). The 2 : 4-*dinitrophenylhydrazone* corresponded with a derivative of the 1 : 2 : 3 : 7 : 8 : 9-hexahydro-ketone and formed very dark red prisms, m. p. 228°, from butanol (Found: C, 64·1; H, 5·8. $C_{21}H_{24}O_4N_4$ requires C, 63·7; H, 6·1%).

In an attempt to isomerise the hydroxy-ketone, 0·1 g. in alcohol (5 c.c.) was treated with potassium hydroxide (0·2 g.) in water (1 c.c.) and refluxed under nitrogen for 2·5 hr. The recovered material, b. p. 115—120°/0·1 mm., crystallised as prisms, m. p. and mixed m. p. 61°, from light petroleum. In the attempted oxidation the hydroxy-ketone (0·2 g.) in benzene (15 c.c.) was refluxed for 5 hr. in the presence of manganese dioxide (1·5 g.) prepared as described by Attenburrow *et al.* (*loc. cit.*). The recovered material crystallised to give unchanged hydroxy-ketone, m. p. and mixed m. p. 59°.

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The Structure of Cyperone. Part III. Natural and Synthetic Cyperones.*

By F. J. McQuillin.

[Reprint Order No. 5527.]

The synthesis of α- and β-cyperone (Adamson, McQuillin, Robinson, and Simonsen, *J.*, 1937, 1576) has been improved so as to lead to the intermediate crystalline ketol (III) in good yield. The configuration of this ketol has been established, as well as those of the optically pure ketones (IV) and (V). Natural α-cyperone is shown to be the 6-epimer of the synthetic (IV). Observations are made on the course of the synthesis and on the mode of racemisation of ketones of type (IV).

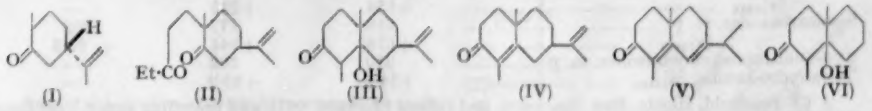
Adamson, McQuillin, Robinson, and Simonsen (*loc. cit.*) prepared synthetic α- and β-cyperones which showed a general correspondence in their properties and in those of their derivatives with natural α-cyperone and the ketone obtained from it by isomerisation. There were, however, differences, ascribed to partial racemisation of the synthetic material. These differences, the later recognition of the "natural" β-cyperone as a mixture (McQuillin, *J.*, 1951, 716), and the uncertainty as to the homogeneity of α-cyperone (cf. Part II *) led us to re-examine this synthesis.

Adamson *et al.* (*loc. cit.*) condensed (−)-dihydrocarvone (I) with diethylmethyl-3-oxopentylammonium iodide in ether–pyridine to obtained a first condensation product consisting largely of a crystalline material, $C_{15}H_{24}O_3$, at that time regarded as the diketone (II). On the basis of a strong hydroxyl absorption at 3510 cm.$^{-1}$ and a typical saturated ketone-carbonyl frequency at 1695 cm.$^{-1}$ this substance must now be given the ketol

* Part II, preceding paper.

structure (III). The conditions for the condensation have been altered so as to afford this crystalline ketol in greatly improved yield and as the main product. An analogous crystalline ketol (VI) has been isolated from a similar condensation with 2-methyl*cyclo*hexanone; Gunstone and Heggie (*J.*, 1952, 1437) failed to observe this. Before discussing the reaction, however, it will be convenient to consider the configuration of the products.

The ketol (III), $[\alpha]_{5461}$ −54°, was smoothly dehydrated in N-aqueous-alcoholic hydrochloric acid at room temperature, or by refluxing in N-alcoholic potassium hydroxide, to give the same unsaturated ketone (IV), $[\alpha]_{5461}$ +210°, +217° (oxime, $[\alpha]_{5461}$ +233°; semicarbazone, $[\alpha]_{5461}$ +244°). From the correspondence in rotation of the ketones and derivatives these preparations are evidently optically pure.



(I) (II) (III) (IV) (V) (VI)

The ketol (III) was not dehydrated by absorption on alumina, or by many hours' refluxing with pyridine and piperidine in benzene or alcohol (cf. Friedman and Robinson, *Chem. and Ind.*, 1951, 777). By treatment with 50% v/v sulphuric acid at room temperature the ketol was dehydrated with concomitant isomerisation to the fully conjugated ketone (V), $[\alpha]_{5461}$ +678° (oxime, $[\alpha]_{5461}$ +307°; semicarbazone, $[\alpha]_{5461}$ +401°), which is regarded as optically pure. Similar acid treatment of the ketone (IV) led to a ketone (V), $[\alpha]_{5461}$ +539°. The ketone (V) of $[\alpha]_{5461}$ +678° was not racemised by this treatment and the reason for this difference is discussed below.

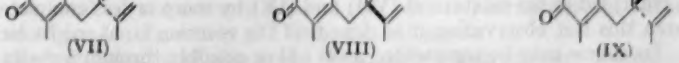
The ketone (IV) on hydrogenation in alcohol gave a tetrahydro-ketone consisting largely of a single crystalline isomer, $[\alpha]_{5461}$ +25·8°, and with lithium in liquid ammonia (Sondheimer, Mancera, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1953, **75**, 1282; Barton, Ives, and Thomas, *J.*, 1954, 903) gave a crystalline dihydro-ketone, $[\alpha]_{5461}$ +25·9°, as sole product and in high yield. Reduction of conjugated steroid-enones by the latter method leads to the stable (*trans*-)bridge-head configuration, and in the present instance this reduction must lead also to the more stable α(equatorial)-configuration for the 4-methyl group. Inspection of the models shows considerable steric interaction in the 4β-methyl configuration with *trans*-ring fusion.

Klyne (*J.*, 1953, 3079) has already indicated that the asymmetry of β-cyperone must be configurationally the same as at the corresponding centre in the steroid molecule. Revised molecular-rotation values based on the optically pure ketones now available are listed in

TABLE 1.

	$[M]_{5461}$	Δ		$[M]_D$	Δ
Dihydrocyperone, synth. ...	+57°	+416°	Cholestan-3-one	+158°	+184°
Synthetic ketone (IV)	+473	+1395	Cholest-4-en-3-one	+342	−1328
Synthetic ketone (V)	+1452		Cholesta-3 : 5-dien-7-one ...	−1170	

Table 1. The configuration of the sterols and terpenes having been correlated (Prelog, *Helv. Chim. Acta*, 1953, **36**, 308 *et seq.*; Mills, *Chem. and Ind.*, 1953, 218; Cornforth, Yenhotsky, and Popjak, *Nature*, 1954, **173**, 536; Arigoni, Riniker, and Jeger, *Helv. Chim. Acta*, 1954, **37**, 878) and the configuration of (−)-dihydrocarvone being known (cf. Hückel,



(VII) (VIII) (IX)

J. prakt. Chem., 1941, **157**, 225; McNiven and Read, *J.*, 1952, 159; Birch, *Ann. Reports*, 1950, **47**, 191), synthetic cyperone may be given the absolute configuration (VII). This synthetic ketone and its derivatives, the natural cyperone, and the earlier synthetic material of Adamson *et al.* (*loc. cit.*) are compared in Table 2. In the absence of any large proportion of the *iso*propylidene isomer (cf. preceding paper) the differences in physical properties

indicated point unmistakably to natural cyperone's being the 6-epimer of the synthetic ketone, *i.e.*, (VIII). The corresponding conformations (X = synthetic and XI = natural) show clearly that the latter represents the more completely "*trans*"-arrangement. The earlier synthetic material (Adamson *et al.*, *loc. cit.*) was correctly described as partly racemic.

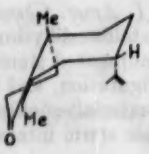
TABLE 2.

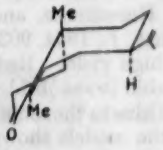
	Natural [1]	Synthetic (*a*)	Synthetic (*b*)
Ketones, $[\alpha]_{5461}$	+119·2°	+216·8°	+58·2° (68°) [2]
n_D^{20}	1·5292	1·5343	1·5299
d^{20}	0·9946	1·006	1·012
Oximes, m. p.	150·5°	90°	144°
$[\alpha]_{5461}$	+134	+233	—
Semicarbazones, m. p.	216	177	202
$[\alpha]_{5461}$	+178	+244	+ 91·5
2 : 4-Dinitrophenylhydrazones, m. p.	210	202	—
Tetrahydro-ketone, $[\alpha]_{5461}$	+14·8	+25·9	—

[1] Cf. Bradfield, Hegde, Rao, Simonsen, and Gillam (*J.*, 1936, 667), and preceding paper. (*a*) Data from this work and (*b*) from Adamson *et al.* (*loc. cit.*). [2] Redetermined in chloroform and, in parentheses, without solvent.

This assignment of the configuration (VIII) to natural cyperone is confirmed unequivocally by other evidence. The crystalline ketol (III) which forms the major product of condensation of (−)-dihydrocarvone and diethylmethyl-3-oxopentylammonium iodide was accompanied by a non-crystalline product, which on chromatography gave a dehydro-ketone corresponding with (IV), but optically impure, $[\alpha]_{5461}$ +42·4°, and affording two oximes, one dextro- and one lævo-rotatory. The latter oxime is clearly derived from the 9-epimer of (VII), *i.e.*, (IX), the enantiomorph of natural cyperone. It

(X)



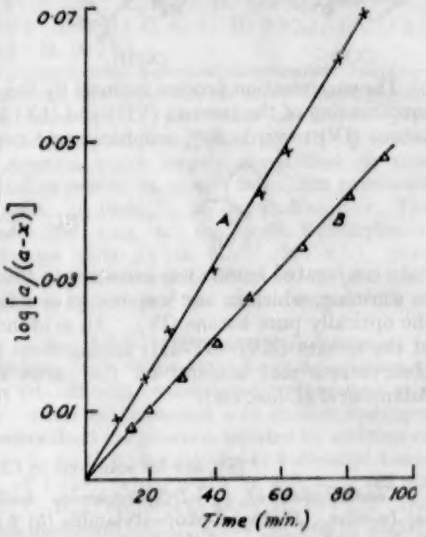


(XI)

was this oxime which Dr. Crowfoot-Hodgkin (cf. Adamson *et al.*, *loc. cit.*) found crystallographically identical with the (dextrorotatory) oxime of natural cyperone. The "identity" is understandable only if the oximes are enantiomorphs, and it provides the strongest support for the configuration assigned to natural cyperone.

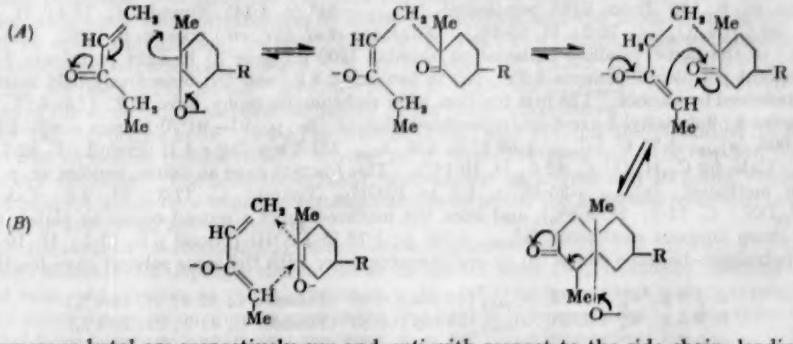
Taken together with the work of Adamson *et al.* (*loc. cit.*) these results throw light also on the course of the metho-salt–sodio-ketone condensation which is the basis of these syntheses. (i) When condensation is carried out in ether (du Feu, McQuillin, and Robinson, *J.*, 1937, 53) with or without a small addition of pyridine (Adamson *et al.*, *loc. cit.*) the metho-salt is insoluble and the reaction is heterogeneous and slow: the yield of condensation product is 30%, including 15—20% of the crystalline ketol (III). (ii) By using sufficient pyridine to ensure rapid reaction in homogeneous medium the total yield is 70%, of which 60% is the ketol (III) in the condensation with (−)-dihydrocarvone; but from 2-methyl*cyclo*hexanone the ketol (VI) was isolated in only small amount. (iii) Whilst mild conditions of dehydration of the cyperone ketol (III) lead, as already noted, to an optically pure dehydro-ketone (VII) the use by Adamson *et al.* (*loc. cit.*) of strong base (dry sodium ethoxide in ether) led to the mixture of (VII) and (IX) by more or less complete inversion at $C_{(9)}$. From this last observation it is clear that the reaction is, as might be expected, reversible. Its course may be represented as in (*A*) or possibly through a cyclic transition state (*B*). The importance of ensuring rapid reaction (and neutralisation) during the condensation is then apparent; not only is the product formed in the initial, kinetically controlled step otherwise inverted to a thermodynamically more stable mixture, but the process is accompanied by loss of yield through self-condensation of the vinyl ketone addend released.

It was noted under (ii) that the 2-methyl*cyclo*hexanone ketol (VI) formed only a minor part of the reaction product, *i.e.*, the ketol is in this case more readily dehydrated. By following the formation of unsaturated ketone from the absorption at 250 mμ it was found, however, that in N-aqueous-alcoholic hydrochloric acid the reverse is the case; the cyperone ketol (III) is the more easily dehydrated (cf. Figure). The *iso*propenyl



Rate of dehydration of ketols in N*-aqueous-alcoholic hydrochloric acid:*
A, the cyperone ketol (III);
B, the ketol (VI).

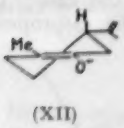
substituent in (III) would be expected to influence dehydration in two ways, (*a*) by facilitating the transition state through increased intramolecular compression, (*b*) by steric retardation of removal of the hydrogen atom or hydroxyl group concerned in the initiating step. The effect of the increased compression should, however, be independent of the initiating step, and we therefore infer that the hydrogen atom and the hydroxyl group in

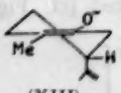


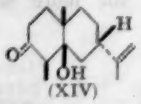
the cyperone ketol are respectively *syn* and *anti* with respect to the side chain, leading to the provisional (*cis*-)configuration (XIV) for this substance.

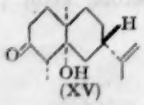
The side-chain substituent also evidently leads to a high measure of stereospecificity in the initial condensation. The sodio-enolate ion of (−)-dihydrocarvone may take up the conformations (XII) and (XIII) of which the former will be the more stable (cf. Barton, Cookson, Klyne, and Shoppee, *Chem. and Ind.*, 1954, 21). With addition predominantly from the side remote from the *iso*propenyl group, these lead to ketols (XIV) and (XV) in proportion to (XII) and (XIII) provided the reaction is sufficiently rapid and is not

reversed. On conversion of the products into the fully conjugated ketones, measurement of rotation shows that the initial reaction is specific to the extent of better than 80% in favour of (XIV).

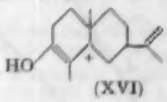

(XII)

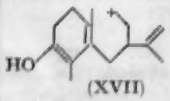

(XIII)

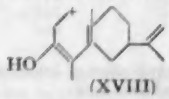

(XIV)


(XV)

The racemisation process induced by the prolonged action of strong base and leading to equilibration of the isomers (VII) and (IX) has a parallel in the behaviour of the synthetic ketone (IV) towards 50% sulphuric acid noted above. The optical purity of the derived


(XVI)


(XVII)


(XVIII)

fully conjugated ketone was sensitive to the conditions of acid treatment and in particular to warming, which in one instance gave a fully conjugated ketone of $[\alpha]_{5461}$ +280·5° from the optically pure ketone (IV). An acid-induced racemisation is understandable in terms of the species (XVI—XVIII) arising from protonation at the carboxyl group, and these observations may account for the partly racemic fully conjugated ketone obtained by Adamson *et al.* (*loc. cit.*).

Experimental

$[\alpha]_D$ are for solutions in $CHCl_3$ unless otherwise stated.

Condensation of (−)-Dihydrocarvone with Diethylmethyl-3-oxopentylammonium Iodide.—(*a*) *In ether.* Diethyl-3-oxopentylamine (51·2 g.) was treated with methyl iodide (46·5 g.) with cooling and rotation of the flask so as to deposit the methiodide on the walls. The sodio-derivative of (−)-dihydrocarvone (62 g.), made from sodamide (18 g.) under ether (700 c.c.), was then added under nitrogen and the mixture stirred in an ice-bath for 6 hr. Next morning the mixture was stirred and refluxed vigorously for 8 hr. The product isolated by addition of water, ether-extraction, and drying, gave on distillation (−)-dihydrocarvone (21·3 g.), followed by material (22·7 g.), b. p. 110—120°/0·1 mm., n_D^{20} 1·5220, which partly crystallised, to give (−)-*decahydro*-10-*hydroxy*-4 : 9-*dimethyl*-3-*oxo*-6-iso*propenylnaphthalene* (3 g.). This formed prisms, m. p. 106° (from light petroleum), $[\alpha]_{5461}$ −54° (*c*, 4·14) (Found : C, 76·1; H, 10·6. Calc. for $C_{15}H_{24}O_2$: C, 76·2; H, 10·2%). Adamson *et al.* (*loc. cit.*) give m. p. 103°. The bulk (14 g.) of the non-crystalline material on alumina (400 g.) gave (i) to light petroleum 2·8 g., (ii) to light petroleum–benzene 3·3 g., (iii) to benzene 2·8 g., and (iv) tenaciously held material, 4 g., removed by alcohol. The first fraction, after rechromatography, gave 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*octahydro*-4 : 9-*dimethyl*-3-*oxo*-6-iso*propenylnaphthalene*, b. p. 91—94°/0·1 mm., n_D^{20} 1·5309, d^{20} 1·006, $[\alpha]_{5461}$ +70·4°, $[\alpha]_{5461}$ +58·2° (*c*, 4·6), $\lambda_{max.}$ 251·5 mμ (log ε 4·1) (Found : C, 82·7; H, 10·0. Calc. for $C_{15}H_{22}O$: C, 82·6; H, 10·1%). This fraction gave an oxime, needles, m. p. 143° (from methanol), $[\alpha]_{5461}$ −25·4° (*c*, 1·7 in EtOH), (Found : C, 77·3; H, 9·8. Calc. for $C_{15}H_{23}ON$: C, 77·3; H, 9·9%), and from the mother-liquors a second oxime as plates, m. p. 130° (from aqueous methanol), $[\alpha]_{5461}$ +78° (*c*, 1·76 in EtOH) (Found : C, 77·3; H, 10·3%). The petroleum–benzene eluate (ii) on rechromatography with the same solvent gave fractions :

(ii) *a*, 1·3 g., n_D^{20} 1·5322, $[\alpha]_{5461}$ (10 cm.) +80° (Found : C, 82·4; H, 10·0%)
b, 0·5 g., n_D^{20} 1·5325, $[\alpha]_{5461}$ (10 cm.) +93° (Found : C, 81·9; H, 10·4%)
c, 0·3 g., n_D^{20} 1·5326, $[\alpha]_{5461}$ (10 cm.) +94° (Found : C, 82·0; H, 10·3%)

i.e., corresponding to 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-oxo-6-*iso*propenylnaphthalene, but containing slightly more of the (+)-isomer. The alcohol eluate (iv) on distillation gave a substance, b. p. 120—130°/0·2 mm., n_D^{20} 1·5276, $[\alpha]_{5461}$ +13·7° (*c*, 4·9) (Found : C, 76·4; H, 9·8. Calc. for $C_{15}H_{24}O_2$, decahydro-4 : 9-dimethyl-10-hydroxy-3-oxo-6-*iso*propenylnaphthalene : C, 76·3; H, 10·2%).

(*b*) *In pyridine–ether.* Diethylmethyl-3-oxopentylammonium iodide (102 g.) in dry pyridine (125 c.c.) was added rapidly with stirring to the sodio-derivative from (−)-dihydrocarvone

(64 g.) and sodamide (18 g.) in ether (400 c.c.). The mixture was stirred at 0° for 12 hr., then heated under reflux for 5 hr. The product was distilled, giving (−)-dihydrocarvone (16·2 g.), followed by material of b. p. 140—150°/0·5 mm. (52·2 g.) which largely crystallised, to give (−)-decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6-*iso*propenylnaphthalene (27·7 g.), a further quantity (3·6 g.) of this ketol being obtained on further distillation and chromatography. From chromatography of the non-crystalline residue were obtained fractions: (i) (7·1 g.), b. p. 87—90°/0·1 mm., n_D^{20} 1·5252, $[\alpha]_{5461}$ (10 cm.) +42·2° (Found: C, 82·0; H, 10·2%); (ii) (4·5 g.), b. p. 91°/0·1 mm., n_D^{20} 1·5272, $[\alpha]_{5461}$ (10 cm.) +70·4° (Found: C, 81·8; H, 9·9%); (iii) (1 g.), b. p. 90—95°/0·1 mm., n_D^{20} 1·5014 (Found: C, 79·3; H, 10·7%).

Condensation of 2-*Methyl*cyclo*hexanone with Diethylmethyl-3-oxopentylammonium Iodide.*—(i) *In ether.* The metho-salt (175·5 g.), treated with the sodio-ketone from 2-methyl*cyclo*hexanone (125 g.) and sodamide (23 g.) in ether (1 l.) and then as above, gave 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-oxonaphthalene (52 g.), b. p. 95—100°/0·5 mm., n_D^{20} 1·5197, followed by a small fraction which largely crystallised, to give *decahydro-10-hydroxy-4 : 9-dimethyl-3-oxonaphthalene* as prisms, m. p. 88°, from light petroleum (Found: C, 73·5; H, 10·4. $C_{12}H_{20}O_2$ requires C, 73·5; H, 10·2%). (ii) *In pyridine–ether.* The metho-salt (184 g.), added in dry pyridine (200 c.c.) to the sodio-2-methyl*cyclo*hexanone from sodamide (23 g.) and the ketone (120 g.) in ether (300 c.c.), gave 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-oxonaphthalene (69 g.), b. p. 90—95°/0·5 mm., n_D^{20} 1·5272. By using ether–alcohol solution, Gunstone and Heggie (*loc. cit.*) obtained 46% of material, b. p. 99—100°/1 mm., n_D^{20} 1·5260.

Dehydration of (−)-*Decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6-iso*propenylnaphthalene.—(i) *With hydrochloric acid.* (−)-Decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6-*iso*propenylnaphthalene (7 g.) in ethyl alcohol (100 c.c.) was treated with concentrated hydrochloric acid (10 c.c.) and kept at room temperature for 60 hr. After neutralisation with sodium hydrogen carbonate solution the bulk of the alcohol was removed and the product, isolated by addition of water and ether, was distilled to give (+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*octahydro-4 : 9-dimethyl-3-oxo-6-iso*propenylnaphthalene (6 g.), b. p. 91°/0·1 mm., n_D^{20} 1·5337, $[\alpha]_{5461}$ +210° (*c*, 3·5), $\lambda_{max.}$ 252 mμ (log ε 4·15 in alcohol) (Found: C, 82·4; H, 10·2. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1%). The *oxime* formed prisms, m. p. 89—90° (from aqueous methanol), $[\alpha]_{5461}$ +233° (*c*, 1·05 in EtOH) (Found: C, 76·9; H, 10·0. $C_{15}H_{23}ON$ requires C, 77·3; H, 9·9%). The *semicarbazone* formed stout rhombs, m. p. 177° (from methanol), $[\alpha]_{5461}$ +244·2° (*c*, 1·1) (Found: C, 69·8; H, 9·3. $C_{16}H_{25}ON_3$ requires C, 69·8; H, 9·1%). The 2 : 4-*dinitrophenylhydrazone* formed scarlet prisms, m. p. 202°, from ethyl acetate (Found: C, 63·0; H, 6·5. $C_{21}H_{26}O_4N_4$ requires C, 63·3; H, 6·5%).

(ii) *With alcoholic potassium hydroxide.* The preceding "cyperone ketol" (3 g.) in 10% alcoholic potassium hydroxide (30 c.c.) was refluxed gently under nitrogen for 8 hr. After dilution with water and neutralisation by dilute hydrochloric acid the product was isolated by means of ether and distilled, to give (+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-*oxo*-6-*iso*propenylnaphthalene (2·5 g.), b. p. 92°/0·1 mm., n_D^{20} 1·5343, $[\alpha]_{5461}$ +216·8° (*c*, 2·2), $\lambda_{max.}$ 252 mμ (log ε 4·23) (Found: C, 82·6; H, 10·4. Calc. for $C_{15}H_{22}O$: C, 82·6; H, 10·1%). This gave the same oxime and semicarbazone as the preparation above.

(iii) The "cyperone ketol" (0·2 g.) in benzene (5 c.c.) with pyridine and piperidine (10 drops each) was recovered quantitatively, having b. p. 110—115°/0·05 mm., m. p. 106°, after 100 hours' refluxing. The same experiment, with alcohol as solvent and 20 hours' refluxing, gave a product which very largely crystallised and from which the ketol was recovered in good yield, m. p. 106°, from light petroleum.

(+)-*Decahydro-4 : 9-dimethyl-3-oxo-6-iso*propylnaphthalene.—(+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-Octahydro-4 : 9-dimethyl-6-*iso*propenylnaphthalene in alcohol with 20% palladised charcoal took up ~2 mols. of hydrogen, to give a product, b. p. 85—90°/0·05 mm., which mainly crystallised and by chromatography on alumina gave in the first light petroleum eluates (+)-*decahydro-4 : 9-dimethyl-3-oxo-6-isopropylnaphthalene* as prisms, m. p. 96° (from light petroleum), $[\alpha]_{5461}$ +25·8° (*c*, 1·74) (Found: C, 81·0; H, 12·0. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%). The 2 : 4-*dinitrophenylhydrazone* formed yellow-orange prisms, m. p. 169°, from ethyl alcohol–ethyl acetate (Found: C, 62·5; H, 7·7. $C_{21}H_{30}O_4N_4$ requires C, 62·6; H, 7·5%).

(+)-*Decahydro-4 : 9-dimethyl-3-oxo-6-iso*propenylnaphthalene.—(+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-Octahydro-4 : 9-dimethyl-3-oxo-6-*iso*propenylnaphthalene (0·5 g.) in dry ether (20 c.c.) was added to a solution of lithium (0·1 g.) in liquid ammonia (150 c.c.) and after 0·5 hr. ammonium chloride (2 g.) was added and the ammonia allowed to evaporate. Recovered by addition of water and ether, the product formed an oil, b. p. 95°/0·1 mm., which crystallised to give *decahydro-4 : 9-di-*

methyl-3-oxo-6-isopropenylnaphthalene, prisms, m. p. 48° (from light petroleum), $[\alpha]_{5461}$ +25·9° (*c*, 3·21) (Found: C, 81·4; H, 11·4. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%). The 2 : 4-*dinitrophenylhydrazone* formed orange-yellow prisms, m. p. 192°, from alcohol (Found: C, 63·0; H, 7·4. $C_{21}H_{28}O_4N_4$ requires C, 63·0; H, 7·0%).

(+)-1 : 2 : 3 : 7 : 8 : 9-*Hexahydro*-4 : 9-*dimethyl*-3-*oxo*-6-*isopropylnaphthalene*.—(i) (−)-Decahydro-10-hydroxy-4 : 9-dimethyl-6-*iso*propenylnaphthalene (0·4 g.) was treated with cold 50% v/v sulphuric acid (5 c.c.) and after 4 hr. the yellow solution was diluted with water and ice. The product recovered by means of ether and washing with water gave (+)-1 : 2 : 3 : 7 : 8 : 9-*hexahydro*-4 : 9-*dimethyl*-3-*oxo*-6-*isopropylnaphthalene*, b. p. 90—95°/0·1 mm., n_D^{20} 1·5632, $\lambda_{max.}$ 301 mμ (log ε 4·44 in EtOH), $[\alpha]_{5461}$ +678° (*c*, 1·44), +672° (*c*, 4·5) (Found: C, 82·7; H, 10·0. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1%). The *oxime* formed prisms, m. p. 139° (from aqueous methanol), $[\alpha]_{5461}$ +307° (*c*, 1·9 in EtOH) (Found: C, 77·5; H, 10·1. $C_{15}H_{23}ON$ requires C, 77·3; H, 9·9%). The *semicarbazone* formed yellow (chromotropic) prisms, m. p. 208° (from methanol), $[\alpha]_{5461}$ +401° (*c*, 1·08) (Found: C, 69·8; H, 9·3. $C_{16}H_{25}ON_3$ requires C, 69·8; H, 9·1%). The "β-ketone" and derivatives described by Adamson, McQuillin, Robinson, and Simonsen (*loc. cit.*) were partly racemic but the melting point of the ketol used was also somewhat low.

(ii) (+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-Octahydro-4 : 9-dimethyl-3-oxo-6-*iso*propenylnaphthalene, $[\alpha]_{5461}$ +210° (1 g.), in 50% v/v sulphuric acid (10 c.c.), as above, gave a (+)-1 : 2 : 3 : 7 : 8 : 9-hexahydro-4 : 9-dimethyl-3-oxo-6-*iso*propylnaphthalene, b. p. 95°/0·1 mm., n_D^{20} 1·5635, $[\alpha]_{5461}$ +539° (*c*, 2·5) (Found: C, 82·8; H, 10·1. Calc. for $C_{15}H_{22}O$: C, 82·6; H, 10·1%).

The author thanks Dr. H. M. E. Cardwell for fruitful discussion and Sir John Simonsen, F.R.S., and Dr. L. N. Owen for samples of natural cyperone and derivatives, and Dr. F. B. Strauss for infrared measurements.

KING'S COLLEGE, NEWCASTLE-ON-TYNE. [*Received, July 6th*, 1954.]

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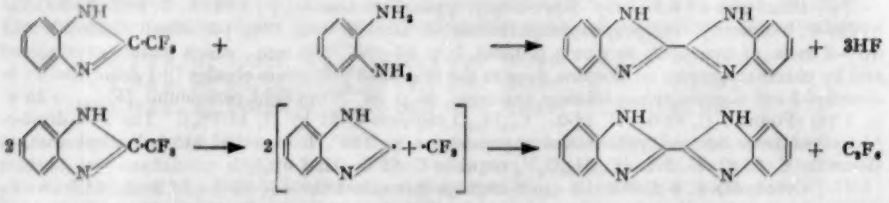
*The Reactivity of the Perfluoroalkyl Groups in 2-(Perfluoroalkyl)-benziminazoles.**

By E. S. LANE.

[Reprint Order No. 5544.]

Examples of a new reaction whereby 2-trifluoromethylbenziminazoles and *o*-diamines give 2 : 2′-dibenziminazolyls are provided. The reaction is extended to 2-heptafluoropropylbenziminazole which also reacts with *o*-phenylenediamine to give 2 : 2′-dibenziminazolyl. The significance of these reactions and some possible mechanisms are discussed.

IT has recently been shown that certain 2-substituted benziminazoles can be prepared by the action of *o*-diamines on carboxylic amides or *N*-2-hydroxyethylamides (Lane, *J.*, 1953, 2238). In an attempt to prepare 2-trifluoromethylbenziminazole by this method from *o*-phenylenediamine and trifluoro-*N*-2-hydroxyethylacetamide a fluorine-free compound was obtained which gave analytical figures corresponding to $C_{14}H_{10}N_4$ and was identified as 2 : 2′-dibenziminazolyl. The following reaction mechanisms could have led to this compound:



Analysis of the reaction mixture gave a 96% overall recovery of fluorine as fluoride ion, so that, in view of the well-known stability of hexafluoroethane, the second mechanism may

* For a preliminary note on some of the work now reported see *Chem. and Ind.*, 1953, 798.

be disregarded. The same reaction also took place between 2-trifluoromethylbenziminazole and *o*-phenylenediamine in boiling ethylene glycol containing 2-hydroxyethylamine as acid acceptor. In a similar manner several 2 : 2′-dibenziminazolyls have been prepared from *o*-diamines and 2-trifluoromethyl-substituted benziminazoles, including, for the first time, some unsymmetrically substituted types; *e.g.*, 5-methyl-2 : 2′-dibenziminazolyl has been prepared from 2-trifluoromethylbenziminazole and 3 : 4-diaminotoluene and also from 5-methyl-2-trifluoromethylbenziminazole and *o*-phenylenediamine. These reactions conclusively support the reaction mechanism proposed above.

The 2-trifluoromethylbenziminazoles required for these syntheses were prepared by conventional methods and show several interesting properties. Microanalyses tended to show high values for hydrogen. Table 1 indicates that progressive replacement of the hydrogen atoms in 2-alkylbenziminazoles by fluorine causes a marked increase in the melting point: association of 1-unsubstituted benziminazoles (Hunter and Marriott, *J.*, 1941, 777), owing to the hydrogen bonding of the 1-hydrogen atoms, can be expected to increase with increasingly acidic nature of the hydrogen atoms involved. The 1-hydrogen atoms in 2-(perfluoroalkyl)benziminazoles are definitely more acidic than those of the corresponding alkyl compounds. Many of them, for example, exhibit an acid reaction in water and some can be titrated with aqueous alkali. The same effect is observed when the 2-positions of two benziminazole ring systems are joined by a (substantially) perfluorinated methylene chain, *e.g.*, in heptafluoroadipoylbis-2-benziminazole. This compound was prepared from heptafluoroadipic acid (from oxidation of intermediates kindly supplied by Mr. E. J. P. Fear, of the Ministry of Supply). The remaining hydrogen atom is believed to be in the α-position. *N*-Methylation of 2-trifluoromethylbenziminazole, however, depresses the melting point to below that of 1 : 2-dimethylbenziminazole, and this is obviously due to the removal of the more powerful counter-effects of the acidic hydrogen atoms and the tautomerism of the system.

TABLE 1. *Melting points of 2-substituted benziminazoles.*

Substituents	M. p.	Substituents	M. p.
2-Trifluoromethyl-	210°	2-Methyl- [1]	175°
2-Pentafluoroethyl- [2]	214—214·5	2-Ethyl- [3]	177—178
2-Heptafluoropropyl-	225—225·5	2-*n*-Propyl- [4]	157—159
Heptafluoroadipobis-2-benziminazole	283	Adipobis-2-benziminazole [5]	259—260
1-Methyl-2-trifluoromethylbenziminazole	97—97	1 : 2-Dimethyl- [6]	110—111

[1] Phillips (*J.*, 1928, 175). [2] Smith, jun., and Steinle, jun. (*J. Amer. Chem. Soc.*, 1952, **75**, 1292). [3] Hinsberg and Funcke (*Ber.*, 1894, **27**, 2189). [4] Weidenhagen (*Ber.*, 1936, **69**, 2763). [5] Shriner and Upson (*J. Amer. Chem. Soc.*, 1941, **63**, 2277). [6] Elderfield and McCarthy (*ibid.*, 1951, **73**, 975).

The well-known effect of the perfluoroalkyl group in reducing the basicity of the heterocyclic nitrogen system into which it is introduced is shown in this series by the failure of 2-(perfluoroalkyl)benziminazoles to form either hydrochlorides or picrates in aqueous solution. In glacial acetic acid crystalline perchlorates are sometimes formed on addition of perchloric acid, but these are not ideal for characterisation since they are frequently thermally unstable. In water, they also revert to the free base.

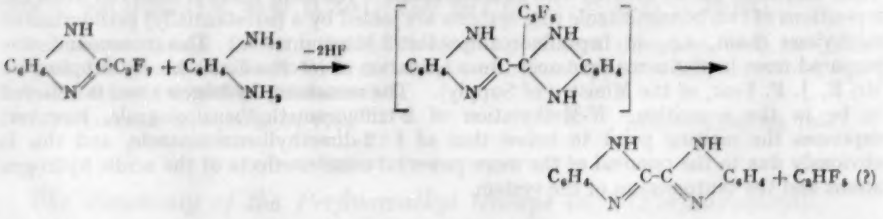
Introduction of the strongly negative trifluoromethyl groups into the 2-position of the benziminazole system does not alter the directing influence of the iminazole ring towards nitration of the benzene ring. Benziminazole itself is normally nitrated in the 5-position (van der Want, *Rec. Trav. chim.*, 1948, **67**, 45; contrast Wooley, *J. Biol. Chem.*, 1944, **152**, 225). 2-Trifluoromethylbenziminazole is similarly nitrated in the 5-position, giving a product identical with that formed in the conventional manner from trifluoroacetic acid and 5-nitro-*o*-phenylenediamine.

The new synthesis of 2 : 2′-dibenziminazolyls described above is not, however, of universal application since certain *o*-diamines fail to react in this manner; *e.g.*, 2-trifluoromethylbenziminazole did not react with 5-nitro-*o*-phenylenediamine and 5-nitro-2-trifluoromethylbenziminazole did not react with either *o*-phenylenediamine or 3 : 4-diaminotoluene. The reaction does, however, appear to be the first example of the reaction of a trifluoromethyl

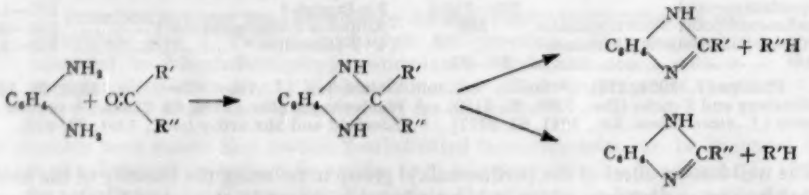
group with primary amines. It also provides a new method for the formation of a benziminazole ring and in this respect should be compared with the preparation of benziminazole itself from *o*-phenylenediamine, chloroform, and potassium hydroxide (Grassi-Cristaldi and Lambardi, *Gazzetta*, 1895, **25**, 225).

The unusual reactivity of the trifluoromethyl groups is probably due to its position adjacent to the nitrogen atom in a heterocyclic base, and provides an interesting parallel to the well-known aldol-type condensations of methyl groups in compounds such as α-picoline, quinaldine, and indeed, 2-methylbenziminazole itself (Bamberger and Berlé, *Annalen*, 1893, **273**, 315).

It was obviously of interest to determine whether the benziminazole ring system altered the reactivity of higher perfluoroalkyl groups in the 2-position. When 2-heptafluoropropylbenziminazole reacted with *o*-phenylenediamine under similar conditions, the product was again 2 : 2′-dibenziminazolyl. Here, in addition to the hitherto unrecorded example of the reaction of primary amine groups with a perfluoroalkyl group it will be noted that a C–C bond in a normally very stable perfluoroalkyl group has been broken. This new reaction is presumed to proceed *via* an unstable intermediate which later disproportionates:



There are certain similarities between this reaction and those leading to benziminazole formation by the reaction of unsymmetrical ketones with *o*-diamines (Elderfield and McCarthy, *J. Amer. Chem. Soc.*, 1951, **73**, 975):



In this case the C–C bond which is broken is the one proceeding from the carbon atom having the greater degree of substitution, so that in the intermediate benziminazoline the pentafluoroethyl group would be expected to be expelled in preference to that of the 2-benziminazolyl residue. Elderfield and McCarthy noticed that *N*-substitution in the *o*-diamine facilitated elimination of the expelled grouping, which is in direct contrast to results in this particular reaction where *N*-substitution completely inhibits the reaction, neither *N*-methyl- nor *N*-phenyl-*o*-phenylenediamine reacting with 2-trifluoromethylbenziminazole. This, however, is probably due to the failure of the initial reaction between fluorine atoms in the perfluoroalkyl group and the hydrogen atoms of the substituted amino-group, so that the unstable benziminazoline structure is not actually formed. Some factors, not yet elucidated, govern the reactivity of amino-groups with perfluoroalkyl groups in this reaction since, although several *o*-diamines have successfully undergone this reaction, no primary aromatic amines have been made to react under these general conditions.

The 2 : 2′-dibenziminazolyls described below contain the same specific grouping as found in the well-known organic reagents for iron, *o*-phenanthroline and 2 : 2′-dipyridyl. None, however, gave colours with iron or with copper salts. Their inactivity is presumably due

to the low basicity of the benziminazole nitrogen atoms and is of interest in view of the recently reported metal-complexing activity of 2-2′-pyridylbenziminazole and 2-2′-pyridyldihydroglyoxaline, both of which possess the same complexing grouping but with one of the heterocyclic nitrogen atoms of the grouping having greater basicity. The failure of the related 2-2′-pyridylbenzoxazole to form complexes with metals has similarly been attributed to the low basicity of the oxazole-nitrogen atom (Walter and Freiser, *Analyt. Chem.*, 1954, **26**, 217).

Experimental

Determination of the Equivalent Weight of Benziminazoles.—(*A*) The 2-(perfluoroalkyl)-benziminazoles can be accurately titrated in dimethylformamide solution with standardised sodium methoxide in methanol–benzene, thymol-blue being used as indicator (Fritz, *Analyt. Chem.*, 1952, **24**, 674).

(*B*) 2 : 2′-Dibenziminazolyls can be accurately titrated with standardised perchloric acid in glacial acetic acid with crystal-violet as indicator (Pifer and Wollish, *ibid.*, p. 300). Dilution of the titration mixture with ether precipitates the perchlorate of the base, which is filtered off. Traces of indicator are removed by washing, and the residue, after drying, is suitable for micro-analysis.

The equivalents recorded below were carried out by these methods. Some compounds were suitable for determination by both methods and the letters in parentheses indicate which particular method has been used in individual cases.

2-Trifluoromethylbenziminazole.—This was prepared by Smith and Steinle's method (*loc. cit.*), except that it was recrystallised from dilute hydrochloric acid; it had m. p. 210° [Found: equiv. (*A*), 186·5. Calc. for $C_8H_5N_2F_3$: equiv., 186]. The *perchlorate* melted at 297° (decomp.) (Found: N, 10·4; Cl, 12·6. $C_8H_6O_4N_2ClF_3$ requires N, 9·8; Cl, 12·75%).

5-Methyl-2-trifluoromethylbenziminazole.—Similarly obtained from trifluoroacetic acid and 3 : 4-diaminotoluene, this *base* crystallised in colourless cubes, m. p. 185·5—187° (from dil. aqueous hydrochloric acid) [Found: N, 14·1%; equiv. (*A*), 199. $C_9H_7N_2F_3$ requires N, 14·0%; equiv., 200].

1-Methyl-2-trifluoromethylbenziminazole.—Similarly prepared from trifluoroacetic acid and *N*-methyl-*o*-phenylenediamine hydriodide (Brown and Le Roi Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 24), this *base* was isolated as colourless diamond-shaped plates, m. p. 95—97° (from aqueous acetic acid) (Found: C, 53·9; H, 4·0; N, 13·9. $C_9H_7N_2F_3$ requires C, 54·0; H, 3·5; N, 14·0%). The *perchlorate* melted at 233—235° (decomp.) (from acetic acid) (Found: N, 9·1; Cl, 12·2. $C_9H_8O_4N_2F_3Cl$ requires N, 9·3; Cl, 12·2%).

5-Nitro-2-trifluoromethylbenziminazole.—(*a*) 4-Nitro-*o*-phenylenediamine sulphate (12·6 g.), trifluoroacetic acid (5·7 g.), and 4N-hydrochloric acid (100 ml.) were refluxed together for 24 hr. After cooling, the solid product was filtered off, including a deposit from the condenser walls (10·5 g.), and the *base* recrystallised from dilute hydrochloric acid in fine, pale yellow needles, m. p. 152—154° (slow heating) [Found: C, 39·5, 39·6; H, 2·4, 2·36; N, 16·5, 16·8%; equiv. (*A*), 250. $C_9H_4O_2N_3F_3.H_2O$ requires C, 38·6; H, 2·4; N, 16·9%; equiv., 249]. It gives a yellow colour with aqueous alkalis.

(*b*) 2-Trifluoromethylbenziminazole (5 g.) was dissolved in concentrated sulphuric acid (25 ml.) and cooled in an ice-bath whilst fuming nitric acid (15 ml.) was added dropwise with efficient stirring. The mixture was kept at room temperature for 2 hr. and then poured into a large excess of cold water. The precipitated solid was filtered off (4·3 g.) and recrystallised from dilute hydrochloric acid. After drying for 2 hr. *in vacuo* at 100°, the *anhydrous* compound melted at 155°. In admixture with the sample (*a*) it melted at 152—154° (Found: N, 17·9. $C_9H_4O_2N_3F_3$ requires N, 18·2%).

4 : 7-Diethoxy-2-trifluoromethylbenziminazole.—Prepared by the procedure detailed above from trifluoroacetic acid and a mixture of 2 : 3- and 2 : 5-diaminoquinol diethyl ether (Lane and Williams, *J.*, 1953, 4187), this *base* melted at 216° (ethanol) [Found: C, 52·7; H, 5·15; N, 10·6%; equiv. (*A*), 276. $C_{14}H_{13}O_2N_3F_3$ requires C, 52·5; H, 4·7; N, 10·2%; equiv., 274].

2-Heptafluoropropylbenziminazole.—Heptafluorobutyric acid (10·7 g.) and *o*-phenylenediamine (5·4 g.) were refluxed together in 4N-hydrochloric acid (100 ml.) for 96 hr. After cooling, *2-heptafluoropropylbenziminazole* was filtered off (5 g.). Further material was obtained by continued refluxing of the mother-liquor but the reaction was very slow. On recrystallisation from aqueous ethanol (charcoal) the base melted at 225—225·5° (with sublimation; in open tube) [Found: C, 42·2; H, 2·8; N, 9·9%; equiv. (*A*), 285. $C_{10}H_5N_2F_7$ requires C, 42·0; H, 1·75; N, 9·8%; equiv., 286].

Heptafluoroadipobis-2-benziminazole.—Heptafluoroadipic acid (5·5 g.) and *o*-phenylenediamine (4·3 g.) were refluxed together for 12 hr. in 4N-hydrochloric acid (25 ml.). The mother-liquor was then decanted from a pale green, plastic residue which gradually became granular on continued trituration in cold water (3·1 g.). The *base*, obtained crystalline with some difficulty on recrystallisation from 50% aqueous acetic acid (charcoal), had m. p. 283° (decomp.) (Found: C, 51·7; H, 3·9; N, 12·8. $C_{19}H_{11}N_4F_7$ requires C, 51·9; H, 2·65; N, 13·5%).

2 : 2′-*Dibenziminazolyl.*—(*a*) Trifluoroacetic acid (11·4 g.) was refluxed for 5 min. with 2-hydroxyethylamine (20 g.); *o*-phenylenediamine (10·8 g.) and ethylene glycol (10 ml.) were then added, and the mixture refluxed for a further 6 hr. during which crystalline material separated out and caused severe " bumping." The contents of the flask were emptied into cold water, and the pale yellow solid which separated was filtered off (9·7 g.). Recrystallisation from ethylene glycol yielded the base in pale, primrose-yellow needles which did not melt at 400° [Found: N, 23·3%; equiv. (*B*), 232. Calc. for $C_{14}H_{10}N_4$: N, 23·9%; equiv., 234].

(*b*) 2-Trifluoromethylbenziminazole (1·86 g.), *o*-phenylenediamine (1·1 g.), and 2-hydroxyethylamine (5 g.) were refluxed together in ethylene glycol (25 ml.) for 6 hr. After cooling, the needle-shaped crystals which had separated were filtered off (1·5 g.) and recrystallised from ethylene glycol, yielding the base (Found: C, 71·5; H, 4·1; N, 24·2. Calc. for $C_{14}H_{10}N_4$: C, 71·8; H, 4·3; N, 23·95%). A similar preparation from 0·400 g. of 2-trifluoromethylbenziminazole was carried out. The reaction mixture was then transferred to a flask and steam-distilled from concentrated sulphuric acid at 140°, and the distillate analysed for fluoride ion by Belcher, Caldas, and Clark's method (*Analyst*, 1952, **77**, 602). The amount of fluoride ion detected was 96% of theory. A duplicate experiment on 2-trifluoromethylbenziminazole indicated that all the fluorine in this compound remained in the covalent form under these experimental conditions.

(*c*) The procedure above was repeated with 2-heptafluorobenziminazole (1·0 g.), *o*-phenylenediamine (0·4 g.), and 2-hydroxyethylamine (0·5 g.). The product was recrystallised from ethylene glycol and did not melt at 400°. It was identified as 2 : 2′-dibenziminazolyl (Found: N, 23·8%; equiv., 233).

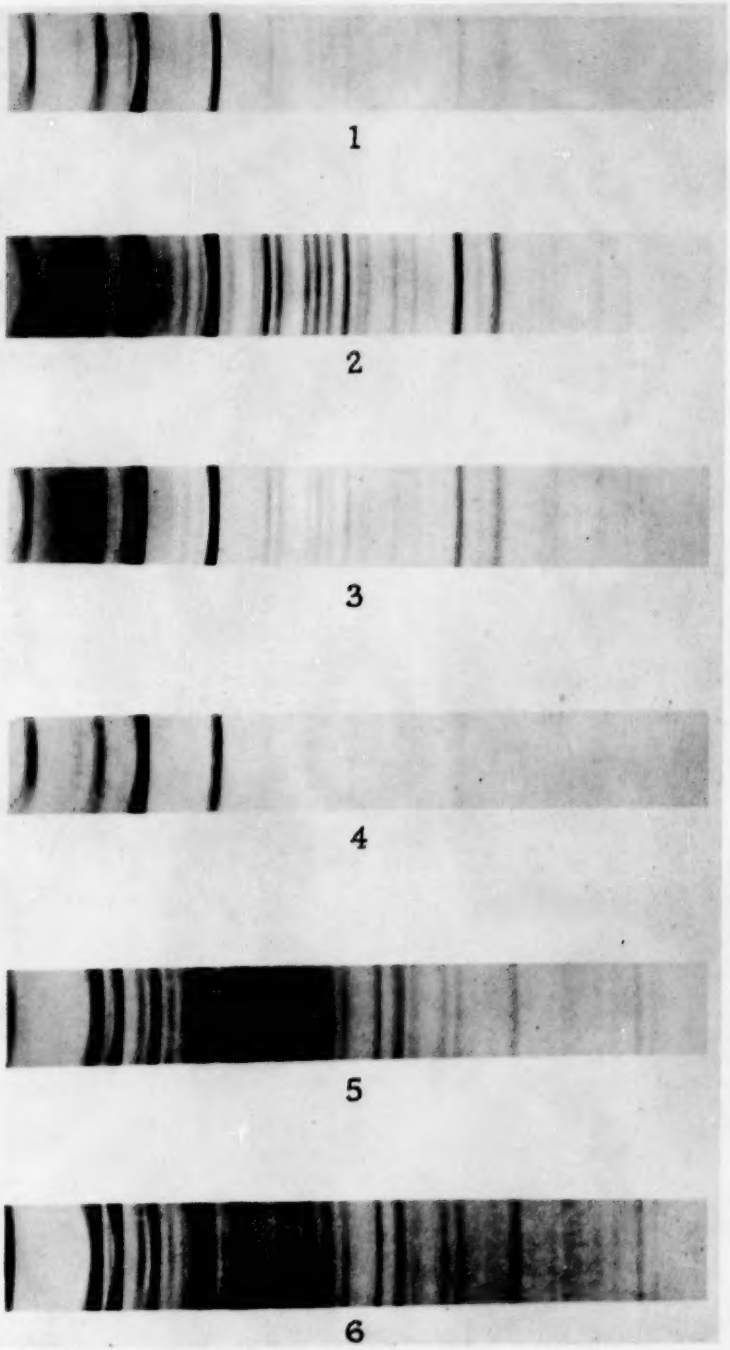
4 : 4′ : 8 : 8′-*Tetraethoxy*-2 : 2′-*dibenziminazolyl.*—2 : 3-Diaminoquinol diethyl ether (Lane and Williams, *loc. cit.*) (1·96 g.), ethyl trifluoroacetate (0·71 g.), and 2-hydroxyethylamine (2 ml.) were refluxed together for 6 hr. (Separation of a crystalline solid caused bumping.) The mixture was poured into water, and the pale yellow solid filtered off (0·9 g.). This highly insoluble material was recrystallised with difficulty from boiling nitrobenzene, the *base* forming a white, microcrystalline powder, m. p. 353° (decomp.), which gave a brilliant orange colour with mineral acids and did not fluoresce under ultra-violet light (Found: C 63·9; H, 6·5; N, 13·9. $C_{22}H_{26}O_4N_4$ requires C, 64·5; H, 6·35; N, 13·7%).

4 : 8-*Diethoxy*-2 : 2′-*dibenziminazolyl.*—Similarly prepared from 2-trifluoromethylbenziminazole (1·9 g.) and 2 : 3-diaminoquinol diethyl ether (2·0 g.), this *base* melted at 352° (decomp.) (from ethylene glycol). It gave orange colours with mineral acids [Found: C, 66·4; H, 5·2; N, 17·7%; equiv. (*B*), 322. $C_{18}H_{18}O_2N_4$ requires C, 67·0; H, 5·6; N, 17·4%; equiv., 322].

5-*Methyl*-2 : 2′-*dibenziminazolyl.*—(*a*) Prepared as above from 2-trifluoromethylbenziminazole (1·86 g.) and 3 : 4-diaminotoluene (1·22 g.), this *base* formed pale yellow crystals (from aqueous alcohol), melting indistinctly at >390° with decomposition and sublimation [Found: C, 71·6; H, 5·15; N, 21·9%; equiv. (*B*), 246. $C_{15}H_{12}N_4$ requires C, 72·5; H, 4·8; N, 22·6%; equiv., 248]. This compound is remarkably soluble in alcohol compared with the related symmetrical compounds 2 : 2′-dibenziminazolyl and 5 : 5′-dimethyl-2 : 2′-dibenziminazolyl (Lane, *loc. cit.*). Acid solutions of the base showed a vivid blue fluorescence under ultra-violet light. The *diacetate* was obtained on crystallising the base from glacial acetic acid as pale yellow needles without a definite m. p. (Found: C, 62·0; H, 5·0; N, 15·2. $C_{15}H_{12}N_4.2C_2H_4O_2$ requires C, 61·9; H, 5·4; N, 15·2%).

(*b*) This was also prepared as above in quantitative yield from 5-methyl-2-trifluoromethylbenziminazole (2·0 g.) and *o*-phenylenediamine (1·1 g.) and identified as the diacetate (Found: C, 62·4; H, 5·45; N, 15·2%).

Characterisation of 2 : 2′-*Dibenziminazolyl and* 5-*Methyl*-2 : 2′-*dibenziminazolyl.*—In view of the unusual nature of the reactions described above it was felt desirable to have as complete a characterisation as possible of these compounds. The former compound for example has no definite m. p. below 400° and is very stable towards common reagents, and the acetates of both compounds are not ideal for characterisation purposes as they have no definite melting point but slowly lose acetic acid on heating. Dr. J. Adam kindly took a number of *X*-ray powder photographs of these compounds, using a 19-cm. camera with filtered Cu-K_α radiation. The Plate shows the powder diffraction patterns obtained, and despite the poor crystallinity of some



1, 2 : 2′-Dibenziminazolyl prepared by Hübner's method (*loc. cit.*).
2, 2 : 2′-Dibenziminazolyl, from $CF_3 \cdot CO_2H$, $NH_2 \cdot CH_2 \cdot CH_2 \cdot OH$, and o-$C_6H_4(NH_2)_2$.
3, 2 : 2′-Dibenziminazolyl, from 2-trifluoromethylbenziminazole and o-$C_6H_4(NH_2)_2$.
4, 2 : 2′-Dibenziminazolyl, from 2-heptafluoropropylbenziminazole and o-$C_6H_4(NH_2)_2$.
5, 5-Methyl-2 : 2′-dibenziminazolyl acetate from 5-methyl-2-trifluoromethylbenziminazole and o-$C_6H_4(NH_2)_2$.
6, 5-Methyl-2 : 2′-dibenziminazolyl acetate from 2-trifluoromethylbenziminazole and 3 : 4-diaminotoluene.

[*To face p.* 538.

of the specimens there is little doubt as to the identity of the samples. 2 : 2′-Dibenziminazolyl prepared by the reactions above shows an identical powder diffraction pattern with that from an authentic specimen prepared by Hübner's method (*Annalen*, 1881, **209**, 339) from *oo*′-dinitrooxanilide. The powder-diffraction patterns obtained from the two samples of the diacetate of 5-methyl-2 : 2′-dibenziminazolyl prepared by the two different methods described above also confirmed their identity.

The author is indebted to Dr. F. Howlett (British Nylon Spinners, Pontypool) who recommended the methods used for the determination of the equivalent weights of these compounds, and to Dr. J. Adam (A.E.R.E.) who took the *X*-ray photographs.

A.E.R.E., Harwell, near Didcot, Berks. [*Received, July 10th*, 1954.]

The Polarized Spectrum of Anthracene. Part I. The Assignment of the Intense Short Wave-length System.

By D. P. Craig and P. C. Hobbins.

[Reprint Order No. 5079.]

Measurements have been made of the absorption spectrum of anthracene crystals between 2800 and 2300 Å, where absorption occurs related to the intense solution band system at 2500 Å. The molecular transition is assigned to the species A_g–B_{3u}, polarized parallel to the long axis.

The interpretation of aromatic crystal spectra is discussed using Davydov's application of Frenkel's exciton theory, and the theory is then used to predict the main features of the crystal band systems corresponding to possible molecular transitions in anthracene. Comparison of these results with the measured spectrum shows that the intense system which has its maximum in solution at about 2500 Å is split in the crystal into two components. One, at 2700 Å, is polarized along the *b* monoclinic axis. The other, which is much more intense, is polarized in the *ac* plane and has its maximum at a wave-length less than 2340 Å, the limit of the measurements.

The assignment to the species A_g–B_{3u} is based on (i) the much greater *ac* polarized absorption intensity than *b* polarized, (ii) the large Davydov splitting between oppositely polarized components, and (iii) the displacement to short wave-lengths of the mean crystal excitation energy relative to vapour and solution values. In all three there is good agreement between experiment and theoretical expectation for the proposed assignment.

The results agree with the predictions of molecular orbital theory in both LCAO form (Coulson, *Proc. Phys. Soc.*, 1948, **60**, 157) and free-electron form (Platt, *J. Chem. Phys.*, 1950, **18**, 1168). This will be discussed later, in conjunction with results on the long-wave system.

Theory of Light Absorption by Molecular Crystals

1. *Davydov's Theory.*—Many of the outstanding problems in the spectra of aromatic molecules, such as the polarization directions of the light absorbed in the band systems, can in principle be solved by studying the spectra of the molecules in crystals in which they are held in known positions. However, the forces which hold the molecules in their places in the crystal are also responsible for the appearance of new features in the electronic spectra which affect their interpretation, especially in intense systems. This has recently been discussed by Davydov, and a statement of his theory is given in this paper as a preliminary to the analysis of the short-wave absorption spectrum of anthracene crystals in the region 2700—2000 Å. In a following paper the anthracene spectrum near 4000 Å will be analysed and assigned.

The theoretical problem of the energy levels of molecular crystals such as those formed by aromatic molecules was studied by Davydov (see, in particular, *Zhur. eksp. teor. Fiz.*, 1948, **18**, 210; *Akad. Nauk S.S.S.R., Pamyati S.I. Vavilov*, 1952, 197). The theory is an application, to molecular crystals, of Frenkel's exciton theory (*Phys. Rev.*, 1931, **37**, 17; *Phys.*

Z. Sowetjunion, 1936, **9**, 158). For the explanation of our results the theory will be set out briefly, for the original is rather inaccessible.

The simplest model of a molecular crystal is that the individual molecules do not act upon one another. In this *oriented gas model* the energy levels are the same as in an isolated molecule, except that rotational sublevels are missing. This model is useful in weak transitions, but more complex behaviour is manifest in many cases: for example, one finds that, not only the intensity of absorption, but also the wave-length varies for different directions of polarization of the absorbed beam. Davydov therefore discussed what may be called the *weak-coupling model* in which the interaction energy between molecules is assumed to be small compared to the intramolecular energy, so that the molecular electronic structure is essentially undisturbed by crystal formation.

The following notation is used:

φ_k, φ_k'	Antisymmetric wave functions for the k-th molecule in its ground state, and in an excited state, respectively.
$\mathbf{H}_k$	Hamiltonian for the isolated k-th molecule.
w_k, w_k'	Isolated molecule energies in the states φ_k, φ_k'.
$\mathbf{V}_{kl}$	Interaction potential energy between the k-th and l-th molecules.
Φ	Electronic wave function for the crystal.
E	Electronic energy of the crystal.

The interaction energy operator is:

$$\mathbf{V}_{kl} = -\sum_{f,j} Z_f e^2/r_{fj} - \sum_{g,i} Z_g e^2/r_{gi} + \sum_{i,j} e^2/r_{ij} + \sum_{f,g} Z_f Z_g e^2/r_{fg} \quad . \quad . \quad . \quad (1)$$

where f and g are the nuclei, Z_f and Z_g the nuclear charges, and i and j the electrons of the k-th and the l-th molecule respectively. Let the number of molecules be N. The energy levels E and the wave functions Φ are defined by the equation:

$$\sum_{k=1}^{N} (\mathbf{H}_k + \sum_{l>k} \mathbf{V}_{kl})\, \Phi = E\Phi$$

The crystal ground state, Φ_0, goes on infinite separation into N unexcited molecules. In harmony with the weak coupling assumption it is written as a simple product of molecular wave functions.*

$$\Phi_0 = \varphi_1\varphi_2\varphi_3 \ldots \varphi_N$$

According to first-order perturbation theory the energy of the ground state is:

$$E_0 = \sum_{k=1}^{N} w_k + \sum\sum \int \varphi_l\varphi_k \mathbf{V}_{kl} \varphi_l\varphi_k \, d\tau \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The second-order terms are not negligible, but they play no important part in the energy-level splitting which we are to discuss, and their consideration is deferred.

A set of excited states of the crystal may be specified by the property that upon infinite separation the N molecules go into $N-1$ in their ground states and one in an excited state. The zeroth-approximation wave function is:

$$\phi_p = \varphi_1\varphi_2 \ldots \varphi_p' \ldots \varphi_N \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The symbol ϕ is used for the product wave function, and φ is reserved for single-molecule functions. Crystal wave functions based on the elementary product functions (3) take the form:

$$\Phi_r = \sum_{l=1}^{N} a_{rl}\phi_l; \text{ where } \sum_{l=1}^{N} a_{rl}^* a_{rl} = 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Φ_r is one of N crystal excited states all belonging in the weak coupling model to the excitation of one molecule to its excited state φ'. The quantity $a_{rl}^* a_{rp}$ is the probability

* Davydov's formulation allows for electron exchange between molecules. We have omitted this refinement since the exchange terms in the energy are very small indeed.

that the p-th molecule is the excitation "site." Clearly if N is a small number, and the end molecules form a significant proportion of the whole, variations between end molecules and others will have to be allowed for, but if N is large as it is in the practical case we may impose cyclical boundary conditions. Then the coefficients a_{rl} will differ from one another only in their phase factors. Quite generally the coefficients may be obtained in the ordinary way from the secular equation:

$$\det\left\{(\phi_p|\sum\mathbf{H}_k + \sum\sum\mathbf{V}_{kl}|\phi_q) - (\phi_p|1|\phi_q)E\right\} = 0 \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Overlap between the electronic orbits of different molecules being neglected, the diagonal elements are (6*a*) and the others (6*b*), where primed sums omit the excited molecule:

$$\sum_k{}'w_k + w_p' + \sum_k{}'\sum_{l>k}{}'(\varphi_k\varphi_l|\mathbf{V}_{kl}|\varphi_k\varphi_l) + \sum_l{}'(\varphi_p'\varphi_l|\mathbf{V}_{pl}|\varphi_p'\varphi_l) - E \quad . \quad . \quad (6a)$$

$$I_{pq} = (\varphi_p'\varphi_q|\mathbf{V}_{pq}|\varphi_p\varphi_q') \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6b)$$

By subtracting the ground-state energy (2) from the diagonal elements of the energy matrix we derive a secular equation whose roots are the crystal excitation energies. The p-th diagonal element is

$$\Delta w_p + D - \Delta E \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where $\Delta w_p = w_p' - w_p$ and

$$D = \sum_l{}'\left\{(\varphi_p'\varphi_l|\mathbf{V}_{pl}|\varphi_p'\varphi_l) - (\varphi_p\varphi_l|\mathbf{V}_{pl}|\varphi_p\varphi_l)\right\} \quad . \quad . \quad . \quad . \quad . \quad (8)$$

It is well known, following Frenkel, that the exchange of excitation between molecules is formally analogous to the motion of a spinless particle, which has been called the exciton. One might regard the functions ϕ as defining localized exciton sites or orbits and the functions Φ_r as delocalized orbits, corresponding to a range of exciton energies. In analogy with the molecular-orbital theory of electrons the integral D in equation (8) is an exciton "coulomb" energy term, and the off-diagonal integrals (6*b*) exciton "resonance" or "exchange" integrals for an exciton jumping fron one molecule to another.

2. *Application of the Rigid Lattice Theory to Anthracene.*—Again, by following Davydov, the discussion can be reduced to specific terms where the crystal structure is known. The

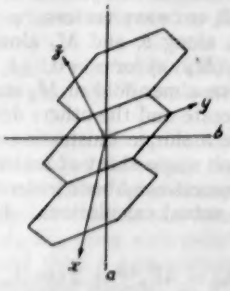


FIG. 1. *Projection of an anthracene molecule on the ab crystal plane.*

(Data from Sinclair, Robertson, and Mathieson, *Acta Cryst.*, 1949, **3**, 251.)

crystals of anthracene belong to the space group C^5_{2h}. The well-defined cleavage plane contains the a and the b monoclinic axis. The c axis makes an angle $\beta = 124°\,42'$ with the a axis and the unit-cell dimensions are $a = 8{\cdot}56$, $b = 6{\cdot}04$, and $c = 11{\cdot}16$ Å. Two molecules occupy the unit cell, at the corner and centre of the ab face. The unit cell group is C_{2h} and one molecule is transformed into the other by reflection in the ac plane followed by translation along the a axis by $a/2$. Fig. 1 shows one molecule of the unit cell projected on to the ab plane of the crystal; this is the cleavage plane normally developed. Fig. 1 also illustrates our convention for molecular axes: the x axis runs in the plane of the molecule parallel to its length and the z axis is perpendicular to the molecular plane. (Some writers reverse the convention.)

The molecular symmetry of anthracene is D_{2h}; the character table for this group is readily accessible and not reproduced here. In the crystal each molecule is at a point in the lattice where the only element of local symmetry is inversion (site group C_i), but the important structural element is now the unit cell and not the molecule, and we shall make no further mention of the site symmetry. The symmetry of the unit cell (group C_{2h}) has the characters given in Table 1. In accordance with the approximation of building crystal wave functions from those for the isolated molecules, combinations of molecular wave functions are formed which transform like representations of the unit-cell group. The necessary relations between the representations of the molecule group D_{2h} and the unit-cell group are also given in the Table. We find, for example, that a molecular B_{2u} state is associated with unit-cell states of both A_u and B_u symmetries.

TABLE 1. *Representations of the unit-cell group* C_{2h}.

	E	C_2^b	i	σ^b	Associated D_{2h} representations
A_g	1	1	1	1	A_g, B_{1g}
$A_u(r_b)$	1	1	−1	−1	B_{2u}, B_{3u}
B_g	1	−1	1	−1	A_g, B_{1g}
$B_u(r_a)$	1	−1	−1	1	B_{2u}, B_{3u}

r_a and r_b denote vectors along the a and the b crystal axis. We now proceed to define unit-cell wave functions γ in terms of the product wave functions ϕ which correspond (3) to excitation of the two molecules in the unit cell individually. The co-ordinate system in one molecule having been chosen, the other is derived from it by glide reflection in the ac plane. We have:

$$\left.\begin{aligned}\gamma^\alpha &= (1/\sqrt{2})(\phi_1 + \phi_2)\\ \gamma^\beta &= (1/\sqrt{2})(\phi_1 - \phi_2)\end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

α and β unit-cell functions formed by combining g molecular wave functions transform like the A_g and B_g crystal species respectively; and those from B_{2u} and B_{3u} molecular functions like B_u and A_u.* N is now assumed large, so that cyclical boundary conditions apply. Wave functions (4) having the symmetry of the three-dimensional space group are:

$$\Phi^{\alpha,\beta}(k_a, k_b, k_c) = (1/\sqrt{N/2}) \sum_{\mu,\nu,\omega} e^{i(k_a a\mu + k_b b\nu + k_c c\omega)}\, \gamma^{\alpha,\beta}(\mu, \nu, \omega) \quad . \quad . \quad (10)$$

k_a, k_b, and k_c are wave vectors. μ, ν, and ω respectively number the M_a unit cells along the a axis, M_b along b, and M_c along c; $M_a M_b M_c = N/2$. The wave vector k_a takes the values $2\pi\sigma/(M_a \,.\, a)$ for $\sigma = 0, \pm 1, \pm 2, \ldots + M_a/2$. For each pair of values of k_b and k_c there is thus a manifold of M_a states, of which those belonging to $k_a = 0$ and $M_a/2$ † are non-degenerate and the others doubly degenerate.

To give a simple illustration of the effects of environment in molecular crystals, we consider one single sheet of molecules in the ab plane and limit ourselves to interactions between nearest-neighbour molecules. As is pointed out below, these restrictions must be relaxed in actual calculations. Denoting the excitation energy of a unit cell by ΔE_u we find:

$$\Delta E^{\alpha,\beta}(k_a, k_b) = \Delta E_u^{\alpha,\beta} + 2\cos(k_a \,.\, a) H_a^{\alpha,\beta} + 2\cos(k_b \,.\, b) H_b^{\alpha,\beta} + 2\cos(k_a \,.\, a + k_b \,.\, b) H_{ab}^{\alpha,\beta}$$

where H_a and H_b are the interactions between neighbour *cells* translationally equivalent along the a and b axes, and H_{ab} is the interaction between neighbour cells displaced along the diagonal. If A, B, and C denote values of the interaction integral (6b) between translationally equivalent *molecules* along the a and the b axis and between the

* Davydov does not use the symmetry properties of the unit-cell wave functions explicitly, and he has a different system of molecular axes. As a result the symmetry species of his α and β combinations are reversed from ours for molecular species B_{1g} and B_{2g}.

† $\sigma = M_a/2$ is non-degenerate for reasons discussed fully by Bethe (*Ann. Physik*, **1929**, **3**, 133). Real functions being used, the cosine function $\Sigma \cos a\mu \,.\, \pi/a$, etc., defines a proper function, but the sine function vanishes identically. Evidently the state $\sigma = M_a/2$ has zero momentum, as has the state $\sigma = 0$.

two molecules of a unit cell we find: $H_a^{\alpha,\beta} = A \pm C/2$, $H_b^{\alpha,\beta} = B \pm C/2$, $H_{ab}^{\alpha,\beta} = \pm C/2$, and $\Delta E_u^{\alpha,\beta} = \Delta w + D \pm C$, where the upper sign applies to α and the lower to β. It now follows that:

$$\Delta E^{\alpha,\beta}(k_a, k_b) = \Delta w + D + 2\cos(k_a \cdot a)A + 2\cos(k_b \cdot b)B \pm \left\{1 + \cos(k_a \cdot a) + \cos(k_b \cdot b) + \cos(k_a \cdot a + k_b \cdot b)\right\}C \quad . \quad . \quad (11)$$

For a chosen set of wave vectors k_a and k_b and a chosen molecular excited state there are two crystal states separated by (12):

$$E^{\alpha}(k_a, k_b) - E^{\beta}(k_a, k_b) = 2C\left\{1 + \cos(k_a \cdot a) + \cos(k_b \cdot b) + \cos(k_a \cdot a + k_b \cdot b)\right\} \quad (12)$$

We shall refer to this interval, calculated for zero values of the wave vectors, as the *Davydov splitting*.

There is a further quantity associated with the energy of the crystal band systems which is of some importance in assigning the transitions and in correlating the crystal absorptions with their vapour and solution analogues. This is the displacement of the mean value of the components ΔE^{α} and ΔE^{β} from the excitation energy in vapour and solution spectra. Anticipating section 3, we note that in the rigid lattice approximation transitions are allowed only for $k_a = k_b = k_c = 0$, and that when lattice vibrations are permitted these transitions will usually still be the most intense. For this case of zero values for the wave vectors the mean transition energy is:

$$(\Delta E^{\alpha} + \Delta E^{\beta})/2 = \Delta w + D + 2A + 2B$$

Δw, the energy of the transition in the isolated molecule, is the vapour transition energy, so that the shift from vapour to crystal is $D + 2A + 2B$. The integral D is capable of approximate calculation. It is the difference between two quantites [see equation (8)] each of which is, in intense transitions, small compared to A and B. We may therefore write for the *crystal shift* the approximate relation:

$$(\Delta E^{\alpha} + \Delta E^{\beta})/2 - \Delta w \cong 2A + 2B \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

We shall apply a relation like (13), suitably generalized to include non-neighbours, only to intense transitions where A and B are of dominating importance compared to D. In weak transitions inclusion of D would be essential.

Table 2 shows that the sum $(2A + 2B)$ can be either positive or negative, leading to the expectation that the crystal shift, in some cases quite large, may be to shorter or longer wave-lengths from the vapour absorption maximum.

3. *Selection Rules and Polarizations.*—The unit cell has a centre of symmetry and, as in the single molecule, the $g \rightarrow u$ selection rule applies. It follows that only those crystal transitions are allowed which correlate with allowed molecular transitions, and their polarizations may be read from the C_{2h} group table. Crystal transitions related either to molecular transitions A_g–B_{2u} (short axis polarized) or A_g–B_{3u} (long axis polarized) have their α components polarized in the *ac* crystal plane, and their β components polarized along the *b* crystal axis. Accordingly the Davydov splitting appears as a separation between a transition polarized along the *b* axis and the corresponding one in the *ac* plane.

The selection rule for the wave vectors k may be deduced from the transition moment integral (14). When expression (10) is used, then

$$\int \Phi_0 \sum_i \mathbf{r}_i \Phi^{\alpha,\beta}(k_a, k_b, k_c)\,d\tau = \sum_{\mu,\nu,\omega} e^{i(k_a a\mu + k_b b\nu + k_c c\omega)} \cdot (2/N)^{\frac{1}{2}} \int \Phi_0 \sum_i \mathbf{r}_i \cdot \gamma^{\alpha,\beta}\,d\tau \quad . \quad (14)$$

The transition moment vanishes unless $k_a = k_b = k_c = 0$. This selection rule applies to the rigid lattice and in this case the crystal band widths suggested by a consideration of the possible ranges of the wave vectors given after (10) are only of formal interest since each molecular transition between pairs of vibronic states gives rise simply to two crystal lines.

Some crystal spectra seem to be of this simple kind but others show evidence of finite band width on account of the excitation of lattice vibrations.

If we use expression (14) to calculate the relative intensities of the *a* and the *b* polarized component of a crystal transition we find that the intensity ratio is unaltered from the oriented-gas model value, and is given by the ratio of the squares of the projections of the active molecular axis upon the crystal axes. This over-simple result is a consequence of the use of first-order perturbation theory. However, the precision of our measured intensities is not enough to justify a more elaborate calculation at this stage.

4. *The Energy Terms.*—We now consider the integrals which occur in the expressions for the splitting and crystal shift. These are of the form (6*b*)

$$I_{lk} = \int \varphi_l' \varphi_k V_{lk} \varphi_l \varphi_k' \, d\tau$$

By expanding the potential (1) in a series of poles of increasing order, and discarding all but the dipole–dipole interactions we obtain (Davydov, *loc. cit.*) :

$$I_{lk} = -(e^2/r^3_{lk})|\boldsymbol{M}|^2 \{2 \cos \theta_{l1} \cdot \cos \theta_{k1} - \cos \theta_{l2} \cdot \cos \theta_{k2} - \cos \theta_{l3} \cdot \cos \theta_{k3}\} \quad . \quad (15)$$

in which $\boldsymbol{M}$ is the molecular transition moment and r_{lk} the distance between the centres of the two molecules. θ_{l1}, θ_{l2}, and θ_{l3} are the angles made by the transition moment of the *l*-th molecule with a set of rectangular axes erected at its centre; θ_{l1} refers to an axis along the line of the centres of the *l*-th and *k*-th molecules. Values of *A*, *B*, and *C* according to equation (15) are given for anthracene in Table 2. The units are cm.$^{-1}$ with the length of the transition moment measured in Å. It is to be noted that according to expression (12) a positive value of *C* means that the *b* polarized component of a transition lies at lower energy than the *ac* component, and *vice versa*.

TABLE 2. *Neighbour intermolecular integrals for crystalline anthracene.*

Integral	Molecular transition Species A_g–B_{3u} (cm.$^{-1}$ Å^{-3})	Molecular transition Species A_g–B_{2u} (cm.$^{-1}$ Å^{-3})
$A/\|M\|^2$	128	49
$B/\|M\|^2$	−739	504
$C/\|M\|^2$	−8	399

It is easy to generalise the results to include non-neighbour interactions. For the allowed transition $k_a = k_b = k_c = 0$ we have, from (10) :

$$\Phi^{\alpha,\beta} = (2/N)^{\frac{1}{2}} \sum_{\mu,\nu,\omega} \gamma^{\alpha,\beta}(\mu, \nu, \omega) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

The energy of the transition to this state may be written in terms of the integrals (6*b*) in the form :

$$\Delta E^{\alpha,\beta} = \Delta w + D + \sum_p I_{lp} \pm \sum_m I_{lm} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (17)$$

where p runs over all molecules translationally equivalent to the *l*-th, and m runs over the others. As before, the upper sign refers to the α wave function and the lower to β. The first sum in equation (17) replaces (and includes) the term $(2A + 2B)$ and the second $4C$ in (12); and both have contributions from non-neighbour interactions. The integrals fall off as the inverse cube of the intermolecular distance and there is some cancellation, leading to a satisfactory convergence when molecules separated by up to 20 Å are included. The individual integrals were evaluated by using expression (15), and the appropriate sums are listed in Table 3, compared with the nearest-neighbour values (shown in square brackets). As in expression (17) the first sum in Table 3 is taken over all translationally equivalent molecules within 20 Å, and the second over the others.

There is a source of error in our values for integrals arising from the fact that

the molecules are not small compared to the lattice spacings, showing that the conditions for cutting off the multipole expansion after the dipole terms are not well realized. Other methods of evaluation, however, are open to the serious objection that they depend on

TABLE 3. *Intermolecular integral sums for crystalline anthracene.*

	Molecular transition Species A_g–B_{3u} (cm.$^{-1}$ Å^{-3})	Molecular transition Species A_g–B_{2u} (cm.$^{-1}$ Å^{-3})
$\sum_m I_{bm}/\|M\|^2$	−990 [−1222]	728 [1106]
$\sum_m I_{am}/\|M\|^2$	96 [−32]	1532 [1596]

assuming specific forms of molecular wave functions; this is an additional uncertainty which it seems best to avoid.

To summarize these results we give in Fig. 2 diagrams of the crystal spectra of molecular transitions of the long- and the short-axis polarized types as deduced by calculation in the dipole–dipole approximation. The molecular transition is assumed to be of intensity $f = 1$, corresponding to $|M|^2 = 2{\cdot}3$.

THE OBSERVED CRYSTAL SPECTRUM OF ANTHRACENE

5. *Preliminary Considerations.*—In solution the two singlet–singlet absorption systems of anthracene in the quartz ultraviolet fall at about 3900 and 2500 Å. The intensity of the first corresponds to an oscillator strength $f = 0{\cdot}1$, and that of the second to $f = 2{\cdot}3$.

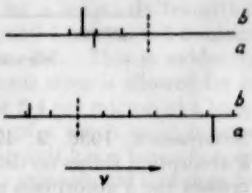


FIG. 2. *Calculated crystal absorption in anthracene corresponding to a single band in the vapour spectrum of a system of intensity $f = 1$. The crystal components are shown by full lines, with the more intense drawn longer; the vapour band is indicated by the broken line. The upper spectrum (showing a red shift and small splitting) is for a short-axis molecular transition and the lower (violet shift and large splitting) is for a long-axis transition. The frequency unit is* 1000 *cm.*$^{-1}$.

It is not to be expected that the properties of the two systems will be entirely independent. The upper state of the weaker system at 3900 Å will be perturbed because the upper state of the stronger gives the weaker band system a composite character, having some properties " stolen " from the more intense system as well as those characteristic of its pure, isolated molecule, species. We believe that the 3900-Å system actually displays such a mixed character, and to distinguish between the two components it is convenient to have established first the properties of the intense system, because this allows the forbidden component to be recognized. For this reason we deal with the intense system first, even though the crystal spectrum is much richer in the 3900-Å region, as will be discussed in a later paper.

6. *Polarization of Absorption Systems.*—The intense system is certainly allowed and may have a transition moment parallel to the x or the y axis, it being assumed to be of the π-π type. At wave-lengths of absorption a single molecule would show strong dichroism; light polarized along the active axis would be absorbed while that polarized at right angles would be transmitted. In crystals the behaviour is less simple because the symmetry elements of the crystal do not coincide with those of the molecules, and because intermolecular forces may change the pattern of energy levels. The purely geometrical effect has already been referred to (Fig. 1). The projection seen by the spectrograph is that shown in Fig. 1, since the *ab* plane is the strongly developed face.* Thus the spectra record absorption of a light beam incident normal to the page with electric vector either parallel to the b crystal axis (b spectra) or perpendicular to it (a spectra). The features to be expected from the effect of intermolecular forces have been discussed in section 1.

* We are indebted to Dr. Philip Knight for several X-ray examinations of crystal flakes of different thicknesses and from different batches. In every case the orientation was found to be (001).

Our method of measurement amounts to finding the optical densities of a thin crystal for light traversing normal to its face and polarized parallel or perpendicular to the *b* axis. The absorption in the 3900-Å system extends to about 3500 Å. Between 3500 Å and the onset of the next system near 2700 Å there is no appreciable structure, but weak and apparently continuous absorption rises to a maximum near 2680 Å, then falls and rises again to a second, lower, maximum at 2595 Å and after that falls slowly. This behaviour is illustrated in Fig. 3. Measurements of these wave-lengths, but not of the optical densities of the absorption maxima, were reported by Obreimov and Prikhotjko (*Phys. Z. Sowetjunion*, 1936, **9**, 49). Their values are in excellent agreement with ours. The *a* absorption shows no definite maximum in this region, but begins to rise near 2600 Å and crosses the *b* absorption near 2540 Å.

FIG. 3. *The weak crystal absorption. Crystal thickness* ~0·1 μ.

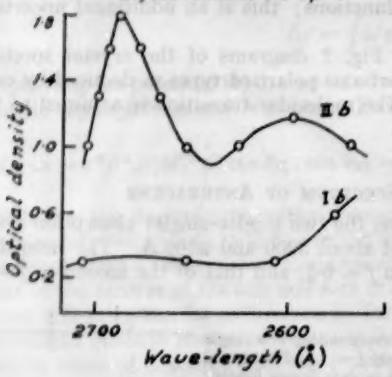
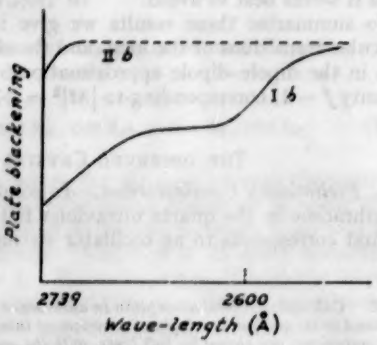


FIG. 4.



I *b*, Perpendicular to *b*; II *b*, parallel to *b*.

Measurements of two crystals of approximately equal thickness are given in the Table.

Optical densities		Wave-lengths (Å)	
E_b	E_a	1st peak	2nd peak
1·79	0·34	2680	2594
1·71	0·29	2678	2595

The optical densities include some loss of light due to reflections from the crystal surfaces. The apparent optical density of a crystal in regions clear of absorption bands is not greater than 0·1 unit, but is too small for accurate measurement by our technique. If a 5—10% reflection loss per surface is assumed, the apparent optical density is in the range 0·04—0·1. We then see that the ratio of absorption optical densities at the maxima is in the region of 7—8 : 1 (the significance of this will be discussed in section 7). The crystals used were about 0·1 μ thick, as determined by microscopy. The spectrum of a crystal several times thicker (Fig. 4) was examined for evidence of an absorption maximum in the *a* spectrum, but none was found.

Toward shorter wave-lengths again, the *a* absorption continues to increase until a cut-off is reached; this happens at about 2300 Å in the thinnest crystals (~0·1 μ). Between 2540 Å and this cut-off point the *b* absorption is less than the *a*, but is rising toward shorter wave-lengths, suggesting the presence of another *b* polarized absorption outside the range of observation. Measurements of the absorption of tetracene crystals, in which the analogous band systems are somewhat shifted to longer wave-lengths, confirm the presence of an intense *b* absorption in this region.

The intensities of absorption in the *b* polarization at 2700 Å and in the *a* polarization at 2300 Å are of considerable importance for the analysis. Values for the former have already

been given, but crystals could not be grown thin enough to enable the maximum at 2300 Å to be located, even with a high intensity arc of the Allen type and very long exposures. In every attempt no more than the onset of the *a* system was penetrated. A conservative estimate is that the *a* system is not less than five times the *b* in optical density.

7. *Discussion.*—To the first order the intensity ratios in crystal spectra are unchanged from the oriented gas values, and the total intensity is the same as that in solution, there being due allowance for random molecular orientation. A satisfactory theory of the crystal absorption must fit both these requirements. We consider first the relation between the solution extinction coefficient of 2×10^5 and the crystal optical densities. Knowing the dimensions of the unit cell and the arrangement of molecules within it we can calculate the optical density per micron thickness of crystal as a function of the solution extinction coefficient for either of the two molecular transition directions, *viz.*:

Crystal axis	Molecular transition	Optical density per micron ($10^{-4}E_s$)
a	Short axis	2·17
b	Short axis	16·9
a	Long axis	5·18
b	Long axis	0·316

The quantity E_s used here is the extinction coefficient in solution, and the conversion factors assume that the shapes of the band systems are not affected by the change from solution to crystal. Setting $E_s = 2 \times 10^5$ we calculate for a short molecular axis transition a *b* crystal optical density of 340 per micron, and for a long axis transition 6·4 per micron. The measured *b* optical density of a crystal about 0·1 micron is 1·8 minus an estimated 0·1 for reflection loss, giving, per micron, the value 17. This is evidently incompatible with the short-axis assignment (calc. 340), but if some error is allowed for in the crystal thickness it agrees as well as can be expected with the 6·4 per micron of a long-axis assignment; moreover the latter leads to the expectation of a much more intense *a* component, again in agreement with experiment, since the long axis has a projection on the *a* crystal axis four times as great as on the *b*, and the intensity ratio should therefore be 16 : 1 in favour of the *a* axis.

We next consider the magnitude of the Davydov splitting, which powerfully supports the long-axis assignment. According to Table 2 and the illustrated spectra of Fig. 2 the splitting is very much greater for a long- than for a short-axis transition. Calculated for an intensity $f = 2{\cdot}3$, the values are 16,000 and 1000 cm.$^{-1}$ respectively. The former agrees satisfactorily with the spectrum: the *b* maximum being taken at 2680 Å, the calculated *a* maximum falls at 1900 Å, which is compatible with *a* absorption beginning strongly near 2300 Å, as is observed. The true maximum is probably a little to longer wave-length of this calculated position. This account of the spectrum implies that in the two regions of crystal absorption the polarization is wholly *b* and wholly *a* respectively. The observed spectrum (Fig. 3) does, however, show some *a* absorption at 2680 Å. We believe that this is not intrinsic to the crystal absorption, but arises from slight distortion of the crystal flakes in the process of mounting (such strains were occasionally seen under the polarizing microscope) and from small errors in aligning the crystal axes with the polarizing directions of the optical system. The alternative explanation of the presence of *a* absorption, that the 2680 Å absorption is a weak short-axis system with little or no Davydov shift, is only doubtfully compatible with the polarization ratio already quoted of 7—8 : 1, as well as being open to objections on other grounds. A value of 7·8 : 1 would indeed be found for a short-axis transition if the molecules were held rigidly in the lattice, but is unattainable in practice. Both torsional oscillations in the lattice and inevitable small errors in alignment reduce the expected value. Torsional oscillations alone (Jablonski, *Acta Phys. Polon.*, 1950, **10**, 193; D. A. Levy, unpublished work) reduce the value to about 7 : 1, and taking account as well of the probable aligning error we consider that 6·5 : 1 is an upper limit to the ratio in a genuine short-axis system. The decisive objection to the short-axis assignment, however, arises from the necessity of accounting in the crystal spectrum for the

same total intensity as in solution. A short-axis system has four-fifths of its intensity in the *b* crystal component and, since the measured *b* optical density per micron is about 17 we could account only for one-twentieth of the solution intensity in this way. There might in fact be a small reduction in intensity in the crystal, but it seems impossible to explain a reduction by a factor 1/20 by using interaction terms of reasonable size.

Finally we consider the wave-lengths of the crystal bands in relation to the vapour and the solution maxima, both of which fall nearly enough at 2500 Å (40,000 cm.$^{-1}$). According to the calculations illustrated in Fig. 2 a long-axis transition is associated with a crystal shift to higher energies, and a short-axis transition to lower energies. There is no doubt that the former agrees with the measured spectrum. The *b* component appears at 37,000 cm.$^{-1}$ and the *a* probably near 50,000 cm.$^{-1}$. The experimental crystal shift is therefore to be measured in thousands of wave numbers, and is toward higher energies. The calculated shift for a long axis system is +4000 cm.$^{-1}$ and for a short axis system −5200 cm.$^{-1}$. The agreement for the former is good, confirming the assignment A_g–B_{3u}.

Our results have a bearing on a problem which has often arisen in discussions of crystal spectra. It has been reported many times that systems which are intense in solution and vapour are greatly weakened in the crystal. Anthracene at first appears to be an example because the weak 2700-Å crystal system lies close to the intense solution absorption and so could be mistaken for the same absorption system simply shifted to the red and much weakened. The explanation is, as we have shown, that the major component of the crystal absorption is found at a wave-length so far displaced that its relation to the solution absorption is not at once suspected. Only the minor crystal component is left close to the solution absorption. An entirely similar explanation applies to the apparent weakening in naphthalene and tetracene, and probably to many of the other cases in the literature.

Experimental

The spectra were recorded on a Hilger large quartz spectrograph E492. Light from a Beckman-type hydrogen lamp was focused on to a crystal of chromatographically purified anthracene mounted over a 1-mm. hole. The transmitted beam was made parallel and passed through a Wollaston prism, then focused on to the slit. The plate recorded two images separated by about 3 mm. for each exposure, corresponding to the two perpendicular directions of plane polarization. The orientation of the anthracene crystal axes was determined with a polarizing microscope, and the crystal was mounted in the optical path with its *a* and its *b* axis respectively parallel and perpendicular to the slit. The crystal holder could be turned through 90° so that errors due to discrimination within the spectrograph between the two beams could be avoided.

The optical densities were measured by sector photometry. On the same plate as the crystal spectrum a series a blank exposures were recorded, each having the same exposure time but different settings of a rotating sector. The blanks recorded optical densities of 0·2, 0·3, up to 1·5, and these were used to determine crystal optical densities essentially by a match-point technique. The crystal spectrum was recorded photographically from the plate on a Zeiss microphotometer, and on the same record traces of the blanks were superposed. Match points corresponded to points of intersection of the blank and the crystal trace. Where necessary, a sector was interposed in the weaker crystal absorption in order to bring the optical density into a more readily measurable range.

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The Mesomorphism of Diisobutylsilanediol.

By C. Eaborn and Norman H. Hartshorne.

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Di*iso*butylsilanediol exists as a mesophase between 89·5° and the m. p., 101·5° (both ±1°). The properties of the mesophase, which is optically negative, cannot be classified unequivocally as smectic, nematic, or cholesteric.

Eaborn (*J.*, 1952, 2840) had observed that di*iso*butylsilanediol, $Bu^i_2Si(OH)_2$, displayed behaviour near its melting point which might indicate a liquid-crystal phase, and we have now confirmed that the substance exists as a mesophase between 89·5° and the melting point, 101·5° (both ±1°). Melting is accompanied by formation of a liquid decomposition product, presumably a siloxane, but the presence of this does not appear to have much effect on these transition temperatures. The properties of the mesophase do not allow it to be classified unequivocally as smectic, nematic, or cholesteric, if the characteristics of these groups are as defined and described by Friedel (*Ann. Phys.*, 1922, **18**, 273). Thus, although it shows some optical phenomena which superficially resemble those associated by Friedel with smectic phases, it is optically negative, and this, according to his classification, should place it at once in the cholesteric group. It shows, however, none of the other characteristic properties of cholesteric phases, such as optical rotatory power, and the display of iridescent colours. The molecular structure of di*iso*butylsilanediol would not lead one to expect a mesophase, whether nematic, smectic, or cholesteric, according to generalisations based on mesomorphic substances previously described (see, *e.g.*, Bernal and Crowfoot, *Trans. Faraday Soc.*, 1933, **29**, 1032).

The di*iso*butyl compound is apparently alone among reported dialkylsilanediols in giving a mesophase. Di-*n*-propyl-, di-*n*-butyl-, di-*tert.*-butyl-, di(trimethylsilylmethyl)-, diallyl-, dibenzyl-, diethyl-, di*iso*propyl-, and di*cyclo*hexyl-silanediols, for example, are all reported as showing normal behaviour on melting (George, Sommer, and Whitmore, *J. Amer. Chem. Soc.*, 1953, **75**, 1585; Sommer and Tyler, *ibid.*, 1954, **76**, 1030; Okawara, Hashitani, and Watase, *Bull. Chem. Soc. Japan*, 1953, **26**, 279; Robison and Kipping, *J.*, 1912, **101**, 2142; Eaborn, *loc. cit.*), and we have confirmed that the last three substances, and also di-*o*-tolylsilanediol, do not exhibit mesomorphism. Several silanediols containing aryl groups have also been reported without mention of unusual behaviour on melting (see, *e.g.*, Robison and Kipping, *loc. cit.*; Cusa and Kipping, *J.*, 1932, 1040; Gilman and Dunn, *J. Amer. Chem. Soc.*, 1951, **73**, 5077; Eaborn, *loc. cit.*). Dimethylsilanediol is described by Kantor (*J. Amer. Chem. Soc.*, 1953, **75**, 2712) as melting at 100—101° after previous shrinkage at 96°, behaviour which might suggest formation of a mesophase but may simply arise from the volatility of this diol, or its instability to heat, and we have been unable to detect any positive evidence of mesomorphism in this compound. (However, when the crystal is heated there is an interesting development, meriting closer study, of what are apparently retreating growth steps on the crystal surface.) *tert.*-Butylhexadecasilanediol, although stable, is reported as melting over a range of 40—45° (Sommer and Tyler, *loc. cit.*).

Experimental

For the study of the mesophase, the electrically heated stage already described by one of us (N. H. H.), and fitted to a Swift "Lapidex" polarising microscope, was used (Hartshorne and Roberts, *J.*, 1951, 1101). This stage permits interference figures of the heated specimen to be obtained. Photomicrographs were taken with a Leitz "Makam" camera attachment.

Much of the optical crystallographic work on the crystalline phase was done on single crystals mounted on a single-axis rotation apparatus (to be described elsewhere), a mounting technique being used based on that of Wood and Ayliffe (*J. Sci. Instr.*, 1935, **12**, 194). In this way different sections of the crystal could be readily brought perpendicular to the axis of the microscope, while the crystal was immersed in a liquid of known refractive index. The rotation apparatus was fitted to a Cooke "Research" polarising microscope.

Diisobutylsilanediol.—The preparation of this substance has been described by Eaborn (*loc. cit.*). *X*-Ray examination and most of the optical work were carried out on samples crystallised from light petroleum, but the larger crystals examined were obtained by slow evaporation of a solution in methanol.

Cryoscopic measurements show that the association factor in benzene is 1·6 (molal concentration, 0·017), and in naphthalene 1·15 and 1·2 (molal concentrations, 0·035 and 0·088, respectively), so that, although the diol shows a strong tendency to associate, it exists substantially in the monomeric form in naphthalene.

The stability of dialkylsilanediols has recently been discussed by Sommer and Tyler (*loc. cit.*); the di*iso*butyl compound is distinctly more stable than diethylsilanediol since it can be recrystallised satisfactorily from high-boiling solvents (*e.g.*, water or nitromethane), or precipitated unchanged by acid from its alkaline solutions, but it is less stable than di*iso*propyl- and di*cyclo*hexyl-silanediols since it decomposes fairly readily when melted.

The Crystalline Phase.—Di*iso*butylsilanediol crystallises from solution in light petroleum or methanol, and from the mesophase between a slide and cover slip, as fine bladed needles with a negative sign of elongation, *i.e.*, the axis of elongation is the " fast " direction of vibration. The growth from the mesophase is usually spherulitic and the radiating bundles of needles often show marked curvature (Fig. 1). The needles have a very pronounced cleavage parallel to the needle axis (Fig. 8), and possibly also an imperfect transverse cleavage, since when pressure is applied to them they break readily along lines of fracture which are often nearly straight and at right angles to the needle axis, in addition to cleaving into numerous individuals parallel to this axis: $\alpha = 1{\cdot}476$, $\beta = 1{\cdot}487$, $\gamma = 1{\cdot}489$, and the dispersion to within 0·001 is negligible; $2V = 43° \pm 2°$ and the sign is negative; α is nearly parallel (within *ca.* 2°) to the needle axis.

We are indebted to Professor J. D. Bernal, F.R.S., Dr. H. Carlisle, and Miss Abd el Rahim, of the Birkbeck College Crystallography Laboratory, for a preliminary *X*-ray examination of the crystals. They find that the symmetry is triclinic, with $a = 14{\cdot}79$ (or possibly a multiple), $b = 5{\cdot}06$, $c = 28{\cdot}82$ Å, and interaxial angles $\alpha \approx 90°$, $\beta \approx 121°$, and $\gamma \approx 96°$ (b = the needle axis). A " sharpened " Paterson projection suggests that the *iso*butyl chains are lying approximately parallel to the γ vibration direction, *i.e.*, perpendicular to the needle axis. This could mean that the molecules are arranged in chains, ··HO–Si–OH···HO–Si–OH····, which are parallel to the needle axis, and this is supported by the fact that the b spacing is very near to that given by Kakudo and Watase for the monoclinic diethylsilanediol [$b = 4{\cdot}97$ Å; *Technol. Reports Osaka Univ.*, **1952**, **2**, (50), 247] in which they find that chains as above and parallel to the b axis occur. Moreover, Kakudo, Kasai, and Watase (*J. Chem. Phys.*, **1953**, **21**, 1894) report a similar b spacing (4·95 Å) and a similar molecular arrangement for diallylsilanediol. These authors consider that the OH···HO linkages are due to interaction between the opposed OH dipoles, (X).

(X)

Kakudo and Watase (*loc. cit.*) find that the silicon–hydroxyl chains in diethylsilanediol are packed side by side in such a way as to form layers which are parallel to the *ab* plane, and consist essentially of planes of oxygen atoms sandwiched between planes of silicon atoms and, outside these, planes of ethyl groups. The Patterson projection for this compound and that obtained for di*iso*butylsilanediol show similarities which are consistent with (though they do not prove) the existence of analogous layers in the latter compound, *i.e.*, layers parallel to the silicon–hydroxyl chains, and the outer " surfaces " of which consist of *iso*butyl groups. This would make the direction normal to the layers the γ vibration direction (see above).

Kakudo and Watase also report the optical properties of diethylsilanediol: the sign is negative as for the di*iso*butyl compound, but the vibration directions corresponding to the two largest principal refraction indices, β and γ, lie in the *ab* plane instead of in a plane normal or nearly normal to *b* as in di*iso*butylsilanediol. This indicates that the arrangement of the molecules into layers parallel to the *ab* plane in the diethyl compound is its dominant structural feature optically. In di*iso*butylsilanediol, on the other hand, if we assume that its structure is essentially the same, the different optic orientation shows that the dominant structural feature is the presence of the large *iso*butyl side groups on the silicon–hydroxyl chains, which makes the polarisability for light vibrating normally to the chains greater than that for light vibrating parallel thereto. A similar effect is found in fully acetylated or nitrated cellulose.

Optical properties for diethylsilanediol have also been reported in a later paper by George, Sommer, and Whitmore, the optical examination having been carried out by M. L. Willard (*J. Amer. Chem. Soc.*, **1953**, **75**, 1585). These authors appear to have been unaware of the

FIG. 1. *Spherulite of crystalline phase.*
Crossed Nicols. × 25.

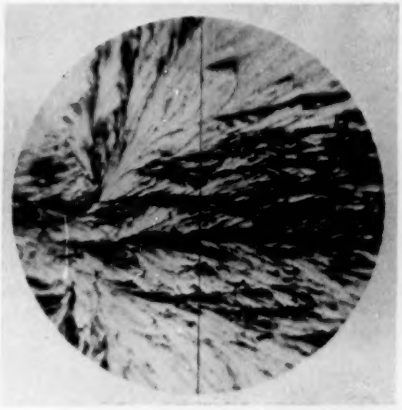

FIG. 2. *Striated band structures obtained by heating spherulite in Fig.* 1.
Crossed Nicols. × 25.

FIG. 3 *Striated band structures.*
Crossed Nicols. × 115.

FIG. 4. *Striated band structures.*
Crossed Nicols. × 174.

FIG. 5. *Bâtonnets.*
Crossed Nicols. × 25

[*To face p.* 550.

FIG. 6. *Bâtonnets.*
Crossed Nicols × 115.

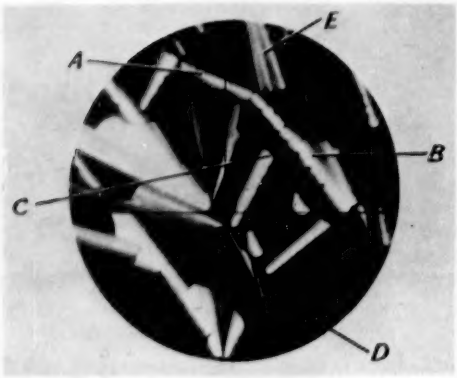

FIG. 7. *Bâtonnets in Fig. 6.*
Polarised light. × 115.

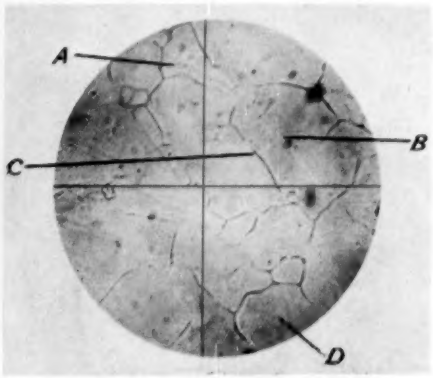

FIG. 8. *Large single crystal showing longitudinal cleavage.*
Crossed Nicols. × 25.

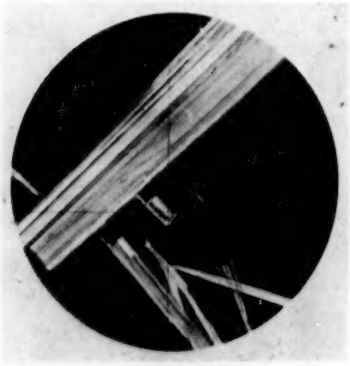

FIG. 9. *Striated band formed from crystal in Fig. 8.*
Crossed Nicols. × 25.

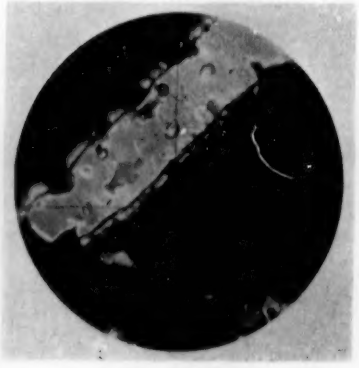

FIG 10. *"Scalloped" structure.*
Crossed Nicols. × 25.

work of Kakudo and Watase. There are considerable discrepancies between their values for the α and γ indices and for $2V$ and those of Kakudo and Watase, and the symmetry is given as orthorhombic. However, they, too, find the sign to be negative and, after allowance for a different choice of axes, the same optic orientation.

The Mesophase.—Fig. 1 is a photomicrograph taken between crossed Nicols of a typical spherulite of crystalline di*iso*butylsilanediol prepared by melting the substance between a slide and cover-slip and allowing it to cool. The mesophase first appears as " bâtonnets " (see below), and on further cooling a spherulitic growth of the crystalline phase occurs. Fig. 2 shows the mesophase obtained from this spherulite by raising the temperature to the mesomorphic region. It will be seen that the original pattern of the spherulite is broadly preserved, but that the acicular crystals give place to bands which between crossed Nicols appear to be transversely striated, and to which we shall refer in the sequel as the " striated band structure." Figs. 3 and 4 show examples of this structure at greater magnification. The striated appearance is due to variations in the extinction directions of successive small portions of the bands. These variations are mostly within the range of a few degrees, and the " fast " direction is always the one parallel or more nearly parallel to the direction of elongation of the bands, so that the latter as a whole have a negative sign of elongation like the crystals from which they were formed It will be observed that the bands do not maintain a constant width, and in this they differ from the " stries huileuses," described by Friedel (*loc. cit.*) and first observed by Lehmann, with which they might at first have been identified for these too are striated and have a " fast " length. (" Stries huileuses " are birefringent bands sometimes produced when the focal conic structure in a smectic phase between a slide and cover-slip is broken up by agitating the cover-slip.) However, Friedel states that under a sufficiently high magnification, " stries huileuses " can be seen to contain chains of minute focal conic structures, and we have always failed to find any definite evidence in the form of unmistakable ellipses and hyperbolæ of the existence of such structures either in the striated bands or in any other mesomorphic preparation of di*iso*butylsilanediol. Some parts of the structures in Fig. 3 do, however, recall the "eventail" type of smectic structure described by Friedel (*loc. cit.*).

When di*iso*butylsilanediol is completely melted between a slide and cover-slip and allowed to cool, the mesophase appears in a dendritic form which at first sight might be mistaken for a dendritic habit of a truly crystalline phase, since the branches are quite straight. Further examination shows, however, that the angles between the branches vary widely whereas they would have a constant value in a crystalline dendrite; secondly, that the branches are apparently rounded in section with no sign of plane faces; and lastly, that when pressure is applied to the cover-slip the structure flows and takes up new forms. Figs. 5 and 6 show examples of this structure at different magnifications. For convenience, and by analogy with the elongated objects which separate from the liquid phase on cooling in the case of ordinary smectic substances, we shall refer to the branches of this structure as " bâtonnets." The extinction along the " spine " of a bâtonnet is usually sharp and straight, and this is the " slow " direction of vibration. In some cases *two* parallel dark lines very close together instead of one dark strip are seen when the " spine " is in extinction. The extinction on either side of this central strip is usually slightly oblique and not quite complete.

Owing to the low birefringence of di*iso*butylsilanediol the polarisation colours shown by both the crystalline phase and the mesophase when prepared as a thin film between a slide and cover-slip are usually not higher than first-order grey and white. The photomicrographs referred to so far lose little, therefore, by being in monochrome and give a very good impression of what is actually seen under the microscope: the bâtonnets, for example, look just like the sections of bright steel tubing, or parts of mediæval armour that the photographs suggest.

A careful optical examination of the bâtonnets has shown that their apparently rounded cross-sectional shape is, to a large extent at least, an illusion. The following observations show that the gradual fall in polarisation colour from white down the middle to grey or black at the edges is mainly or wholly due to a change in orientation of the internal structures rather than to a decrease in thickness. In convergent light between crossed Nicols, the dark borders show centred or nearly centred negative uniaxial interference figures, and as the spine of the bâtonnet is approached the inclination of the optic axis (or acute bisectrix; see below) of the structure steadily increases and so, therefore, does the birefringence of the medium for normally incident light. In some bâtonnets the optic axis becomes inclined towards the spine, with reference to the direction of vision; in others, away from it. The two cases are, of course, the same structure, the one being merely the other in an inverted position.

The spine of the bâtonnet appears to mark a discontinuity in the structure, since when

the analyser is removed the spine can be resolved as a faint dark or bright line (depending on the position of focus of the microscope tube). Thus in Fig. 7, which shows the same subject as Fig. 6 but with the analyser removed, the spines of the bâtonnets *A* and *B* can be clearly traced, and those of others also. Fig. 7 also shows that the boundary line between two bâtonnets meeting at an angle is in equally sharp focus throughout its length (*e.g.*, the boundary *C*), showing that it does not vary appreciably in height as it would do if the bâtonnets were rounded in section. There is some variation in relief along the line, but this is to be expected since the relative orientations of the structures, and therefore the difference between their refractive indices, are not the same at all points. (A high-aperture, 4-mm. objective was used for these observations, with a depth of focus much less than the distance between the slide and cover-slip, so that very small changes of level in the bâtonnets could have been detected.)

Between the bâtonnets are domains which between crossed Nicols remain in extinction in all positions of rotation of the microscope stage, *e.g.*, domain *D* in Figs. 6 and 7. These domains give centred, negative, uniaxial, interference figures, and thus correspond to the homeotropic structure in ordinary smectic phases, except for the optical sign.

Two other features of the bâtonnets may be mentioned : (i) It has often been observed that interference figures obtained near the spine are slightly biaxial, suggesting that here there is some distortion of the structure which prevails elsewhere. (ii) The bâtonnets frequently show what appears to be a notched ornamentation at or near the edges : this is seen on some of the bâtonnets in Fig. 6. The structural significance of this feature is not clear.

When the cover-slip on a bâtonnet preparation is moved laterally, the whole structure moves bodily with it, so that there appear to be no linkages with the slide. This may be due to the cover-slip's being at a slightly lower temperature than the slide so that the bâtonnets form in the first instance on the cover slip and then subsequently remain isolated from the slide by a thin layer of the liquid decomposition product.

To sum up, the bâtonnet structure consists of domains probably showing little or no variation in thickness, separated by boundary surfaces or thin junction zones of some kind (possibly analogous to the zones of focal conics, which according to Friedel, *loc. cit.*, connect differently oriented homeotropic regions in an ordinary smectic phase). In some of these domains the optic axis is perpendicular to the glass surfaces throughout. In others (the so-called bâtonnets) the optic axis is progressively inclined towards a straight central surface or junction zone (the " spine ").

The striated band structure and the bâtonnet structure are not, as their appearance might suggest, distinct mesophases each with its own temperature range of stability, since if we start with the striated band structure and raise the temperature until the bands are partially melted, and then lower it, bâtonnets grow into the liquid as continuations of the striæ. Again, we have made preparations under a temperature gradient, containing both striated bands and bâtonnets, and no phase boundary between the two structures could be seen. The two structures appear to be able to intermingle freely without change. Moreover, portions of bâtonnet structures are often seen which are indistinguishable from the striæ in the band structure, as for example domain *E* in Fig. 6. Thus it may be supposed that a striated band consists essentially of a succession of small bâtonnets linked side by side.

Experiments on Large Single Crystals.—When the mesophase is prepared between a slide and cover-slip either as striated bands or as bâtonnets and is then allowed to cool, crystallisation occurs from a number of centres as spherulites as already mentioned. These spherulites rapidly invade and replace the mesomorphic structure, and the orientation of the latter appears to have no effect on that of the crystals. A different result is obtained if a large single crystal (obtained from solution) is slowly heated and cooled between a slide and a cover-slip. In this case, the crystal (Fig. 8) becomes a striated band (Fig. 9), and on cooling, crystallisation of this band takes place as an interface reaction to give a single crystal with the original orientation. There is some change of shape as compared with the original crystal because of sublimation on to the cover-slip during the process and possibly because the fluid mesophase suffers some deformation as a result of the pressure of the cover-slip. A noteworthy phenomenon accompanying these changes is that the polarisation colour of the mesophase as a whole is distinctly lower than that of the original crystal, and that on recrystallisation of the mesophase the original colour is regained. Thus, in one example studied, the original and the final crystal showed a strong first-order orange, and the mesophase a pale yellow, corresponding to a fractional fall in relative retardation of about one-quarter.

Discussion

If optically negative silicon–hydroxyl chains packed side by side to form layers exist in the crystalline state, as is suggested by the *X*-ray evidence, there appear to be two main alternative possibilities regarding the structure of the mesophase, one involving a parallel association of chains, and the other a system of parallel layers, and these will be discussed separately.

(1) The first possibility (which at first sight is the more attractive since it involves the smaller *internal* disturbance of the structure) is that the mesophase consists essentially of a parallel or near-parallel association of silicon–hydroxyl chains with a random lateral arrangement, so that the layer structure of the crystal is not preserved. The chain direction which is the acute bisectrix (α) in the crystal thus becomes the optic axis of the uniaxial mesophase, and since for both phases this is the vibration direction corresponding to the smallest refractive index, no pronounced change in the optical properties of the medium is involved in passing from one phase to the other. Silicon–hydroxyl chains, which in the crystal are held together primarily by van der Waals forces (if Kakudo and Watase's smallest oxygen–oxygen distances between neighbouring chains in diethylsilanediol, *viz.*, 3·64 Å, are applicable in the present case), simply become loosened from one another, but preserve their parallel or a near-parallel arrangement. Difficulties are, however, involved in this simple picture, and it is not adequate to explain all the properties of the mesophase, as the following considerations show. In the first place it would imply that the cross-sectional structure of the bâtonnets is as depicted in Fig. 11 (*a*), where the lines drawn between the upper and the lower surface represent the mean directions of the chains. This in turn would mean that the chains, which in the crystal are endless and lie parallel to the glass supporting surfaces, break up into finite lengths and orientate themselves obliquely or normally to those surfaces when the temperature reaches the mesomorphic region. This at once raises the question as to whether the presence of the glass surfaces, or one such surface, is essential for the development of the mesomorphic structures which we have described. One possibility that suggests itself is that the endless chains break as a result of the input of thermal energy, and then the end Si–OH groups attach themselves firmly to the glass by interaction with its Si–O linkages. The following experiments show, however, that the glass does not play an essential rôle. (*a*) When an uncovered crystal is laid across a small hole etched in a cover-slip and is heated, it becomes a striated band bridging the hole. In other words, this characteristic structure is formed where the substance is not in contact with any solid surface at all. (*b*) Crystals heated on a film of rhombic sulphur supported on a slide develop the striated band structure apparently just as readily as on glass.

One phenomenon has been observed in which the presence of a glass surface does appear to have an effect on at least the coarser details of the mesomorphic structure. In the experiment just described of heating a crystal laid across a hole, it is frequently seen that the parts of the crystal in contact with the glass adopt a convoluted shape, which we will call the " scalloped " structure, when the mesophase forms. In some cases the part of the crystal which was over the hole withdraws to the side of the hole, and the whole crystal then develops the scalloped structure. A rather poor example of this is shown in Fig. 10. The hole in the glass can just be discerned below the middle part of the mesophase.

The mere requirement that the silicon–hydroxyl chains remain parallel would give us a phase with typical nematic properties; it is evident that we are dealing with something which is structurally more restricted than that, and if parallel chains are present there must also be some additional restraint on the system. The formation of bâtonnets from the liquid phase instead of the spherical anisotropic drops which appear in the case of nematic substances may be cited as probably the strongest argument against classifying di*iso*butylsilanediol as nematic.

(2) The second possibility is that the system of parallel layers in the solid crystal is preserved in the mesophase and is the cause of the optically negative character of the

latter. The optic axis must now be normal to the layers, whereas in the crystal this direction was γ, the approximate direction of the *iso*butyl chains. Furthermore, the layers must become singly refracting for this direction of propagation, since the mesophase is uniaxial. Thus in passing from the crystalline phase to the mesophase, the vibration direction corresponding to the greatest refractive index becomes that corresponding to the smallest refractive index. To account for this and for the change to uniaxial character it would seem necessary to suppose that quite considerable changes in the bonding within the layers, and in the inclination of the *iso*butyl chains to the layer planes, occur, but since the birefringence of the crystalline phase is small (0·013) the structural changes necessary on passing to the mesophase need not be prohibitively large. The fact that just such a difference in optic orientation exists between crystalline di*iso*butyl- and diethyl-silanediol, as mentioned earlier, emphasises this point if, as we have been assuming, their structures are indeed similar. What is not so easy to understand is how layers consisting of silicon–hydroxyl chains, linked laterally by van der Waals forces, can become isotropic for normally incident light when the temperature is raised. The change would appear to require the breakdown of the hydrogen bonding of the chains to give place to

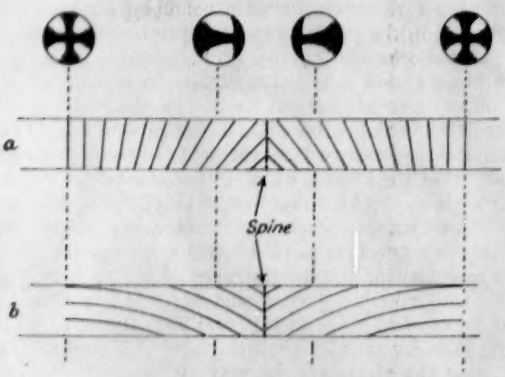

FIG. 11. *Possible cross-sectional structures of a bâtonnet with typical interference figures shown by different parts.*

The vertical and sloping lines in (a) *represent the mean directions of silicon–hydroxyl chains. The curved lines in* (b) *represent layers.*

a statistically non-directional interaction (within the planes of the layers) between the hydroxyl groups, sufficiently strong to hold each layer together.

If the mesophase possesses such a layer structure, there will be much less disturbance of the crystal structure when transformation of this to the mesophase takes place than that which, as we have seen, must be supposed to occur if the structure of the mesophase is based on possibility (1). Regions of the crystalline phase in which the layers are already parallel to the glass surfaces can easily form homeotropic domains giving centred uniaxial figures in the mesophase and birefringence will be favoured wherever the layers are tilted with respect to the glass surfaces, though the cause and exact nature of the relationship between the crystal and mesophase orientations must for the present remain obscure, particularly as the glass surfaces appear to play little or no part in determining the latter. The cross-sectional structure of a bâtonnet might be as depicted in Fig. 11 (*b*).

The fall in polarization colour observed when a single crystal passes into the mesophase agrees with expectation for both the chain and layer pictures. In both cases the changes in optical properties and orientation are such that the directions of propagation corresponding to low or zero double refraction tend to be normal to the plane of the slide.

Proof of the presence of layers in the mesophase would go some way towards accounting for its pseudo-smectic properties, and it is hoped that future work will yield more information about this, and other details of its structure. It may then prove possible to identify it with one of the 18 geometrically possible states intermediate between true liquids and true crystals which have been conceived on theoretical grounds by Hermann (*Z. Krist.*, 1931, **79**, 186).

We are grateful to Professor J. D. Bernal, F.R.S., and Dr. C. H. Carlisle for their interest and comments. We thank Imperial Chemical Industries Limited for the loan of the "Cooke" Research Polarizing Microscope and the Leitz "Makam" Camera Attachment with the aid of which much of the experimental work described in this paper was carried out.

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Kinetic Studies of the Oxidation of Aromatic Compounds by Potassium Permanganate. Part I. Toluene.

By C. F. CULLIS and J. W. LADBURY.

[Reprint Order No. 5477.]

A kinetic investigation of the oxidation of toluene by potassium permanganate is described. Under the conditions used, attack occurs mainly at the methyl group, resulting in stepwise oxidation of toluene to benzoic acid. Simultaneously, some disruption of the aromatic ring takes place, but this does not appear to occur during the initial oxidation of toluene itself, being associated only with the further oxidation of certain intermediate products formed.

The dependence of initial oxidation rate on hydrogen-ion concentration is complex, but the reaction is of the first order with respect to both potassium permanganate and toluene. Nevertheless, studies of the effect of complex-forming agents and other added salts show that the greater part of the oxidation is done by Mn^{3+} or associated ions, and that the reaction does not involve to any great extent direct oxidation by the MnO_4^- ion.

A CHARACTERISTIC reaction of the monoalkylbenzenes is their oxidation to benzoic acid. In preparative work, alkaline permanganate is often used to oxidise the alkyl side-chains. A kinetic investigation must, however, be made in acid solution, since aqueous acetic acid is the only suitable solvent. The present paper deals with the reaction of toluene with potassium permanganate; the oxidation of related compounds will be discussed in subsequent papers.

In an early kinetic investigation of the oxidation of aromatic compounds by permanganate, Hinshelwood (*J.*, 1919, 1180) studied the effect of substitution on the oxidation of phenols. Hinshelwood and Winkler (*J.*, 1936, 368, 371) showed that the simple second-order behaviour observed could only be explained on the basis of a reaction between a phenol molecule and the permanganate ion. No simple relation was found between the activation energies and velocity constants. Alexander and Tompkins (*Trans. Faraday Soc.*, 1939, **35**, 1156) found sigmoid reaction–time curves at low acidities for the oxidation of 2 : 6-dinitrophenol in presence of sulphuric acid, the sigmoid character being ascribed to catalysis by the Mn^{2+} ion. These authors suggested that intermediate manganese ions are involved, and that the principal oxidising species is the hydroxyl radical produced by the reaction, $Mn^{3+} + H_2O \rightleftharpoons Mn^{4+} + OH + H^+$. Tompkins (*ibid.*, 1943, **39**, 280) outlined the distinguishing features of oxidations involving on the one hand the permanganate ion and on the other intermediate manganese ions.

With the phenols, the aromatic ring is completely oxidised to carbon dioxide. With toluene and its homologues oxidation of the side chain takes place preferentially, although some ring rupture often occurs concurrently. The only previous kinetic study of the reaction of the toluenes with permanganate is that of chlorotoluenes by Speroni and Barchielli (*Gazzetta*, 1941, **71**, 765), who found that the oxidations are of the second order and are not autocatalytic : no carbon dioxide was evolved, which implies that the aromatic ring remains intact.

Ions derived from every valency state of manganese from 7 to 3, as well as the hydroxyl

radical, have been suggested as responsible for the oxidising action of potassium permanganate. In this investigation, the oxidation cannot be attributed to any single species, but the Mn^{3+} ion is believed to be one of the most important entities involved.

Experimental

Materials.—All the organic compounds used, with the exception of acetic acid, were purified by conventional methods. The acetic acid was of "AnalaR" grade and was not specially purified. The inorganic compounds were "AnalaR" materials or of comparable purity. Solutions of benzyl alcohol and benzaldehyde were stored in an atmosphere of carbon dioxide.

Kinetic Measurements.—In the majority of experiments, reaction was followed iodometrically. Manganese dioxide is the end product of permanganate reduction, and is deposited during the reaction. It was therefore necessary to use separate vessels for each determination, and Y-vessels with a total capacity of about 60 ml., in which the solutions of the two reactants could be brought separately to the required temperature and then mixed, were used throughout.

If a is the initial concentration of permanganate in moles/l., x is the number of moles of permanganate per l. consumed in time t, $1/p$ is the normality of the thiosulphate used to titrate the iodine liberated by the residual permanganate and manganese dioxide formed, v is the volume of reacting solutions, and N' and N are the number of ml. of thiosulphate required after respectively zero time and time t, then $x = (N' - N)/3vp$, and $(a - x) = (5N - 2N')/15vp$.

Method of obtaining Initial Rates.—In most cases, no simple kinetic law is obeyed throughout the reaction, and the velocity constants cannot be determined by application of an integrated rate equation to the experimental results. Only initial rates were therefore considered. A convenient method of finding these is to plot x/t against x and to extrapolate to $x = 0$ (Hinshelwood, *loc. cit.*; Fudge and Sykes, *J.*, 1952, 119); where this method was used, satisfactory linear plots were obtained for about the first 20% of reaction. Not all the results were amenable to this procedure and in some cases resort had to be made to measurement of initial tangents to the reaction–time curves.

Small corrections were made for oxidation of the acetic acid, which is appreciable in certain cases. Since the solvent is present in large excess, its oxidation is effectively of the first order with respect to the permanganate only. A correction may thus be applied by subtraction from the initial total rate of reaction of the product of the previously determined first-order rate constant and the initial permanganate concentration.

Estimation of Evolved Carbon Dioxide.—Measurements were made of the fraction of aromatic compound oxidised to carbon dioxide during the reaction. "Oxygen-free" nitrogen was passed first through soda-lime and then into the reacting solutions. It was then bubbled into saturated aqueous barium hydroxide contained in three wash-bottles connected in series. After reaction was complete, the barium carbonate was filtered off, dried, and weighed. Blank experiments were performed to allow for oxidation of the acetic acid.

Sources of Error.—(i) Autoxidation of benzaldehyde and other intermediates may cause the rates of reaction in presence of air to differ from those in absence of oxygen. However, when the reaction was carried out in an atmosphere of carbon dioxide, no differences in rates could be detected. No precautions were therefore taken to exclude air from the reaction solutions in subsequent experiments.

(ii) No allowance was found to be necessary for the very slow oxidation caused by manganese dioxide.

(iii) Correction was made for the contraction in volume which occurs when glacial acetic acid and water are mixed.

Products of the Oxidation of Toluene.—An equimolar mixture of toluene and potassium permanganate in 54·2% w/v acetic acid was allowed to react with vigorous stirring for 4 hr. at 50°. After the manganese dioxide had been deposited from the solution, the clear supernatant liquid was decanted off and extracted repeatedly with ether. The manganese dioxide sludge was also treated with ether in a Soxhlet apparatus. The ether extracts were combined and washed with water, and the water washings were found to contain only acetic acid. The ether was next washed with 10% sodium hydroxide solution and then contained only neutral compounds. The alkaline extract was acidified and extracted with ether; the latter then contained the acidic products. The neutral extract was shown to contain only benzaldehyde (m. p. of 2 : 4-dinitrophenylhydrazone 236°, lit. 237°) and unchanged toluene (b. p. 110°, lit. 110°). No

benzyl alcohol, dibenzyl, or benzyl acetate could be detected. When the ether extract containing the acid constituents was evaporated, white crystals were obtained, insoluble in cold water and soluble in hot water. These were recrystallised from water and had m. p. 121° which was unaltered on admixture with authentic benzoic acid (lit., m. p. 121°). The mother-liquor from these crystals was tested for the presence of phenols with diazotised *p*-nitroaniline; only a very faint coloration was observed.

Results and Discussion

Evolution of Carbon Dioxide.—The extent of complete disruption of the aromatic ring, as disclosed by the evolved carbon dioxide, is illustrated in Table 1.

Table 1.

Temp.: 50°. Solvent: 54·2% w/v aqueous acetic acid. $[PhCH_3] = 0{\cdot}0103$M; $[KMnO_4] = 0{\cdot}103$M.

$PhCH_3$ taken (g.)	Weight (g.), corrected for oxidation of solvent, of $BaCO_3$	CO_2	Ph·CH_3 completely oxidised (%)
0·0921	0·0981	0·0219	7·1
0·0921	0·0961	0·0214	6·9

Stoicheiometry.—The oxidation of toluene by permanganate probably proceeds through the stages: $Ph{\cdot}CH_3 \longrightarrow (Ph{\cdot}CH_2{\cdot}OH) \longrightarrow Ph{\cdot}CHO \longrightarrow Ph{\cdot}CO_2H$, each of which involves one atom of oxygen (or two-thirds of a molecule of permanganate) provided no side reaction occurs. Inability to detect benzyl alcohol in the product is not readily explicable, though it may be due, at least partially, to the insensitivity of the α-naphthyl *iso*cyanate test. It is interesting that Slack and Waters (*J.*, 1948, 1666) could not isolate diphenylmethanol after oxidation of diphenylmethane by chromic acid.

The amounts of permanganate needed in practice to oxidise toluene, benzyl alcohol, and benzaldehyde were determined by allowing the compounds to react with an eight-fold excess of oxidising agent until the residual oxidising power of the solution showed only a slight decrease with time characteristic of the rate of oxidation of benzoic acid and of the solvent. The results are given in Table 2, together with the theoretical quantities needed

Table 2.

Temp.: 50°. Solvent: 54·2% w/v aqueous acetic acid. [Organic compound] = 0·00517M; $[KMnO_4] = 0{\cdot}0413$M.

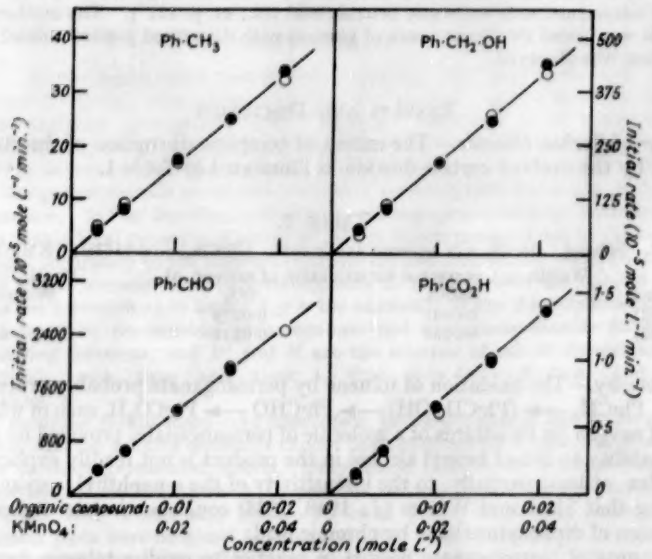
		$PhCH_3$	Ph·CH_2·OH	Ph·CHO
Moles of $KMnO_4$ reqd. to oxidise 1 mole:	Found ...	2·89	2·23	1·28
	Theor. ...	2·00	1·33	0·67

for oxidation of the side chain only. The differences may be ascribed to concurrent ring rupture, and show that, with toluene, 8·9% is completely oxidised to carbon dioxide; this value may be compared with 7·0% obtained from direct measurement of the carbon dioxide evolved (Table 1). The amounts of benzyl alcohol and benzaldehyde oxidised to carbon dioxide are 9·0% and 6·1% respectively. The fact that the extent of ring rupture of toluene as determined by measurement of the carbon dioxide evolved agrees quite well with the value obtained from the stoicheiometry measurements suggests that the carbon dioxide arises principally from nuclear oxidation of the aromatic compound, and not, for example, from induced oxidation of the acetic acid.

The difference between the experimental values of the stoicheiometry for toluene and benzyl alcohol (Table 2) is 0·66, and corresponds exactly with the theoretical difference. This implies that no appreciable ring rupture takes place in the first stage of reaction. Attack of the ring does occur, however, in the later stages and the carbon dioxide evolved is evidently derived entirely from ring fission during the oxidation of benzyl alcohol and benzaldehyde.

Influence of Reactant Concentrations.—The initial rates of reaction of permanganate with toluene, benzyl alcohol, benzaldehyde, and benzoic acid are all of the first order with respect to each reactant (Fig. 1). Second-order kinetics are not, however, maintained throughout

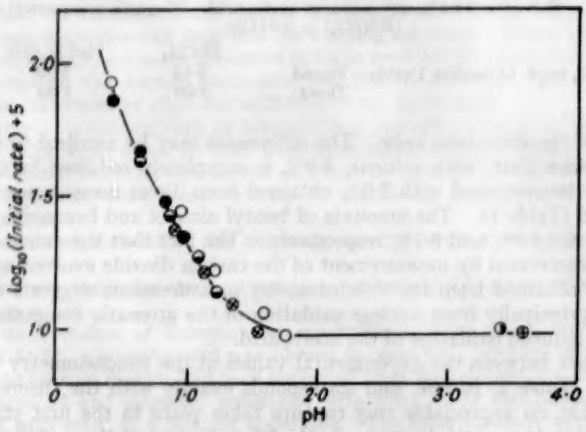
FIG. 1. *The dependence of initial oxidation rate on reactant concentrations.*



Temp.: 50°. Solvent: 54·2% w/v (9·03 moles l.$^{-1}$) aqueous acetic acid.

○ [Organic compound] = 0·01M; [$KMnO_4$] varied.
● [$KMnO_4$] = 0·02M; [Organic compound] varied.

FIG. 2. *The dependence of initial oxidation rate on* pH.



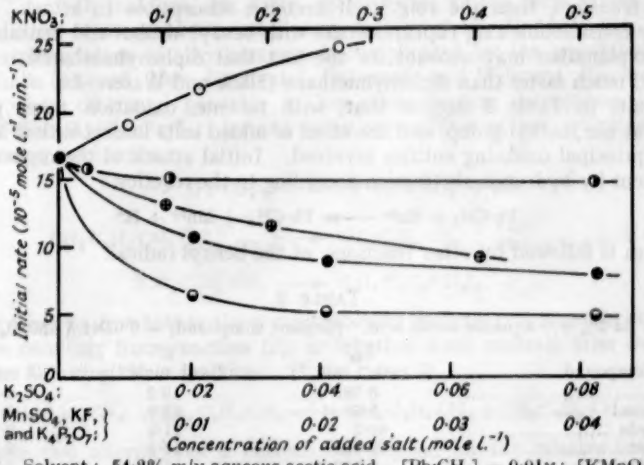
Temp.: 50°. [Ph·CH_3] = 0·01M; [$KMnO_4$] = 0·02M.

○ CH_3·CO_2H.
◑ 1·24M-CH_3·CO_2Na in 9·0M-CH_3·CO_2H.
⊕ 1·24M-CH_3·CO_2Na in 7·3M-CH_3·CO_2H.
● H_2SO_4 in 9·0M-CH_3·CO_2H.
⊖ H_2SO_4 in 7·3M-CH_3·CO_2H.
⊗ H_2SO_4 in 4·4M-CH_3·CO_2H.

the reactions, and with benzyl alcohol and benzaldehyde the reaction–time curves are sigmoid. Second-order kinetics are a common feature of permanganate oxidations (Hinshelwood, *loc. cit.*; Hinshelwood and Winkler, *loc. cit.*; Alexander and Tompkins, *loc. cit.*; Mann and Tompkins, *Trans. Faraday Soc.*, 1941, **37**, 201; Speroni and Barchielli, *loc. cit.*; Hill and Tompkins, *Trans. Roy. Soc. S. Africa*, 1942, **29**, 309; Tompkins, *loc. cit.*), but the simple conclusion that reaction results from a bimolecular interaction between an organic molecule and the permanganate ion is thought not to be correct in the present case.

Hydrogen-ion concentration has a more complex effect on the reaction, and the influence of pH (as measured by a glass electrode) is shown in Fig. 2. Variations in the concentration of acetic acid cause a marked change in rate of oxidation, and it is clear that the principal influence of the solvent lies in its provision of a source of hydrogen ions. The small differences in rate when sulphuric acid and acetic acid are used to produce the same pH may be due to the weak complexing effect of the sulphate ion (cf. Fig. 3).

FIG. 3. *The dependence of initial oxidation rate on added salts.*



Temp.: 50°. Solvent: 54·2% w/v aqueous acetic acid. $[Ph{\cdot}CH_3] = 0{\cdot}01$M; $[KMnO_4] = 0{\cdot}02$M.
○ $MnSO_4$; ◑ KNO_3; ⊕ K_2SO_4; ● KF; ◒ $K_4P_2O_7$.

Influence of Added Salts.—Manganous sulphate reacts with potassium permanganate (Guyard, *Bull. Soc. chim.*, 1864, **1**, 89) to produce intermediate manganese ions such as Mn^{3+} (Bassett and Sanderson, *J.*, 1936, 207); the latter are readily removed by pyrophosphate and fluoride ions by complex formation. If MnO_4^- ions are primarily responsible for the oxidation, a reduction in initial rate should be observed in presence of added Mn^{3+} ions which reduce the concentration of MnO_4^-. If, on the other hand, intermediate manganese ions are the active oxidising species, Mn^{3+} ions should cause an acceleration. Similarly addition of pyrophosphate and fluoride ions should retard reaction if intermediate manganese ions are mainly responsible for oxidation, but should cause no significant change if MnO_4^- ions are the principal oxidising entities. Fig. 3 shows the effect of added salts. Manganous sulphate has an accelerating influence, and the complex-forming agents cause retardation. This suggests that Mn^{3+} and associated ions are the principal species responsible for oxidation. The observed effects are much greater than normal salts effects, as shown by the influence of potassium nitrate. Addition of potassium sulphate causes a slight slackening in rate, probably owing to formation of the complex $[Mn(SO_4)_2{\cdot}2H_2O]^-$ (Ubbelohde, *J.*, 1935, 1605).

Even with a high concentration of pyrophosphate ions, the rate is only reduced to about 30% of the normal value. Ions derived from Mn^{3+} are thus not the sole oxidising entities, though they appear to be the most important species present.

It was found that the presence of the added salts in the concentrations used did not significantly affect the pH of the system, so that the observed changes in oxidation rate cannot be ascribed to a buffering action.

Influence of Temperature.—The initial rates at 50° and the Arrhenius parameters for the reactions of permanganate with toluene, benzyl alcohol, benzaldehyde, and benzoic acid are shown in Table 3 together with data on related compounds.

The closeness of the values of A for the first three compounds is to be expected since in each case attack occurs predominantly at the side-chain; the similar steric factor for benzyl acetate suggests that here too an analogous mode of attack occurs. The lower value for benzoic acid may be attributed to oxidation of this compound only at the aromatic ring.

The comparative ease of oxidation of benzyl alcohol and benzaldehyde (Table 3) may be ascribed to the electro-negative character of the oxygen atom in the side-chain. This and the $-I$ effect of the aromatic ring will both tend to promote ionisation of the hydrogen atoms on the α-carbon atom, so that the excess of negative charge developed can become the centre for oxidative attack. If the charge is dispersed to the ring by the normal tautomeric transfers, then the ring itself becomes susceptible to attack. This would explain why considerable ring rupture occurs with benzyl alcohol and benzaldehyde. An analogous explanation may account for the fact that diphenylmethanol is oxidised by chromic acid much faster than diphenylmethane (Slack and Waters, *loc. cit.*).

The results in Table 2 suggest that, with toluene, oxidation takes place almost exclusively at the methyl group, and the effect of added salts indicates that Mn^{3+} ions are among the principal oxidising entities involved. Initial attack of the organic compound may well occur by hydrogen abstraction according to the reaction:

$$Ph{\cdot}CH_3 + Mn^{3+} \longrightarrow Ph{\cdot}CH_2{\cdot} + Mn^{2+} + H^+$$

which in turn is followed by other reactions, of the benzyl radical.

TABLE 3.

Solvent: 54·2% w/v aqueous acetic acid. [Organic compound] = 0·01M; [$KMnO_4$] = 0·02M.

Compound	k_{50} (l. mole^{-1} min.$^{-1}$)	E (kcal. mole^{-1})	A (l. mole^{-1} min.$^{-1}$)
Toluene	0·785	13·2	$6{\cdot}45 \times 10^8$
Benzyl alcohol	9·60	12·9	$5{\cdot}40 \times 10^9$
Benzaldehyde	60·5	11·8	$9{\cdot}77 \times 10^9$
Benzoic acid	0·029	11·8	$2{\cdot}76 \times 10^6$
Benzyl acetate	0·196	15·7	$7{\cdot}67 \times 10^8$
Dibenzyl	2·82	—	—

After oxidation of diphenylmethane with chromic acid, Slack and Waters (*loc. cit.*) were able to isolate tetraphenylethane and hence to show that hydrogen abstraction from the methylene group takes place to some extent. By analogy, it might be expected that appreciable amounts of dibenzyl would be found among the products from toluene on the basis of the mode of attack proposed. The failure to detect this compound does not, however, form evidence against the reaction postulated, for the dimerisation of benzyl radicals could only occur to a significant extent if subsequent oxidation of such radicals was slow in comparison with their formation.

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The Reactivity of p-*Methylbenzyl Radicals. A Novel Application of the Kinetic Isotope Effect.*

By J. I. G. Cadogan, V. Gold, and D. P. N. Satchell.

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The decomposition of dibenzoyl peroxide in [α-$^2H_1$]*p*-xylene produces 4 : 4′-dimethyldibenzyl containing the statistically expected proportion of deuterium atoms. The result indicates that, under the conditions of the experiment, the reaction of *p*-methylbenzyl radicals with *p*-xylene, $CH_3{\cdot}C_6H_4{\cdot}\dot{C}H_2 + CH_3{\cdot}C_6H_4{\cdot}CH_3 \longrightarrow CH_3{\cdot}C_6H_4{\cdot}CH_3 + \dot{C}H_2{\cdot}C_6H_4{\cdot}CH_3$, occurs much more readily than their dimerisation.

It is well known that the decomposition of dibenzoyl peroxide in an aromatic solvent PhX (where X = NO_2, halogen, Ph, OMe, or H) gives, as the main products, benzoic acid and a mixture of monosubstituted diphenyls (Hey *et al.*, *J.*, 1954, 794, and earlier papers). The phenylation of alkylbenzenes is complicated by the possibility of attack in the side chain (Augood, Hey, Nechvatal, Robinson, and Williams, *Research*, 1951, **4**, 386). Thus, when dibenzoyl peroxide in low concentration decomposes in *p*-xylene solution, 4 : 4′-dimethyldibenzyl is formed to an appreciable extent, which is consistent with the following mechanism :

$$(Ph{\cdot}CO_2)_2 \longrightarrow Ph{\cdot} + Ph{\cdot}CO_2{\cdot} + CO_2 \quad \text{(i)}$$

$$CH_3{\cdot}C_6H_4{\cdot}CH_3 \begin{matrix} + Ph{\cdot} \\ + Ph{\cdot}CO_2{\cdot} \end{matrix} \longrightarrow CH_3{\cdot}C_6H_4{\cdot}\dot{C}H_2 \begin{matrix} + PhH \\ + Ph{\cdot}CO_2H \end{matrix} \quad \text{(ii)}$$

$$2CH_3{\cdot}C_6H_4{\cdot}CH_2{\cdot} \longrightarrow (CH_3{\cdot}C_6H_4{\cdot}CH_2)_2 \quad \text{(iii)}$$

The question arises as to whether the *p*-methylbenzyl radicals concerned in equation (iii) are only those resulting from reaction (ii), or whether fresh radicals arise owing to the presence of the following chain reaction :

$$CH_3{\cdot}C_6H_4{\cdot}CH_2{\cdot} + CH_3{\cdot}C_6H_4{\cdot}CH_3 \longrightarrow CH_3{\cdot}C_6H_4{\cdot}CH_3 + CH_3{\cdot}C_6H_4{\cdot}\dot{C}H_2 \quad \text{(iv)}$$

Which of these two alternatives is correct will depend on the relative importance of hydrogen abstraction and dimerisation as the mode of reaction of the *p*-methylbenzyl radicals under the prevailing experimental conditions. This type of problem cannot be attacked by conventional methods of investigation but, as is now shown, can be solved by application on a hydrogen-isotope technique involving determination of the isotopic composition of the dimer resulting from *p*-xylene of known isotopic distribution.

Experimental

The method of hydrogen-isotope analysis employed has been described by Bryce-Smith, Gold, and Satchell (*J.*, 1954, 2743).

Preparation of [α-$^2H_1$]p-*Xylene.*—*p*-Methylbenzyl alcohol (m. p. 60°), prepared from *p*-toluic acid by reduction with lithium aluminium hydride, was converted into *p*-methylbenzyl bromide (m. p. 35°; 60%) by Kamm and Marvel's method (*Org. Synth.*, Coll. Vol. I, p. 25). The halide (0·23 mole), in ether, was converted into the Grignard reagent from which the deuterated hydrocarbon was prepared by the slow (20 min.; dropwise) addition of deuterium oxide (0·4 mole; 99·7% purity) to the vigorously agitated solution of the Grignard reagent, kept at its b. p. The mixture was stirred for a further 30 min., and solid carbon dioxide was then added in order to remove unchanged Grignard reagent. The mixture was acidified (N-hydrochloric acid) and the layers were separated. The ether solution was successively washed with water, 2N-sodium hydroxide (twice), and water, and dried ($CaCl_2$). Evaporation of the solvent from the filtered solution left a pale yellow oil, which was distilled (helix-packed column). The fraction of b. p. 138°/760 mm. was refractionated from sodium metal to give [α-$^2H_1$]*p*-xylene (yield 60%) of the same b. p., and m. p. 13° (unchanged by

fractional freezing) (Found : D, 6·95. Calc. for C_8H_9D : D, 10·00 atoms %).* A portion of the product was oxidised by alkaline potassium permanganate. The resulting terephthalic acid was found to contain D, 0·47 atom %, indicating the presence of a small amount of deuterium in the nucleus (cf. Bryce-Smith, Gold, and Satchell, *loc. cit.*). On the assumption that no multiply deuterated compounds are formed in the reaction, the composition of the product was therefore : $CH_2D{\cdot}C_6H_4{\cdot}CH_3$, 66·7; $CH_3{\cdot}C_6H_3D{\cdot}CH_3$, 2·8; $CH_3{\cdot}C_6H_4{\cdot}CH_3$, 30·5 mole %.

Decomposition of Dibenzoyl Peroxide in [α-$^2H_1$]p-*Xylene.*—Dibenzoyl peroxide (1·9 g.) was added (10 min.) to the solvent (20 g.) kept at 80° in a thermostat. After 72 hr. the decomposition was considered to be complete and the excess of *p*-xylene was removed by distillation through a helix-packed column. The residual oil was boiled under reflux with 2N-sodium hydroxide (30 ml.) for 8 hr. in order to hydrolyse the esters present. The mixture was extracted with benzene (4 × 20 ml.), and the combined extracts were washed with water and dried ($CaCl_2$). The benzene was removed by distillation (10″ column), and the pale yellow oil distilled *in vacuo*, giving a pale yellow semi-solid product (b. p. 60—90°/0·15 mm.; 1·10 g.). The liquid was removed by filtration through sintered glass, and the solid residue (0·75 g.) was recrystallised to constant m. p. (82°) from aqueous methanol, giving 4 : 4′-dimethyldibenzyl (0·23 g.) in colourless plates. The product contained D, 6·4 ± 0·1 atoms %.

Discussion

When *p*-methylbenzyl radicals are formed by reaction of [α-$^2H_1$]-*p*-xylene with the free radicals resulting from the decomposition of benzoyl peroxide, there is competition between the rupture of C–H and C–D bonds. The theoretical considerations which predict that C–H bonds will break more rapidly than C–D bonds are well known, and have been abundantly verified experimentally—for the particular case of homolytic fission in solution by Kharasch, Rowe, and Urry *J. Org. Chem.*, 1951, **16**, 905). Consequently, the *p*-methylbenzyl radicals formed in the reaction considered would be expected to contain more than the statistically calculated proportion of deuterium. If the dimer is formed by the combination of a pair of this " first generation " of radicals, then it will have the same deuterium content as these radicals. If, on the other hand, dimerisation is very unlikely compared with hydrogen abstraction [equation (iv)] then isotopic equilibrium between the *p*-methylbenzyl radicals and the *p*-xylene may be established, by reactions such as (v), before dimerisation occurs :

$$CH_3{\cdot}C_6H_4{\cdot}CH_2{\cdot} + CH_3{\cdot}C_6H_4{\cdot}CH_2D \rightleftharpoons CH_3{\cdot}C_6H_4{\cdot}CH_3 + CH_3{\cdot}C_6H_4{\cdot}CHD{\cdot} \quad . \quad . \quad (v)$$

If, as would be expected, the equilibrium constants for such reactions are close to unity, isotopic equilibration will result in a statistical distribution of deuterium among the α-hydrogen atoms of the *p*-xylene. It can be shown that, for such a distribution,† the deuterium content of any reaction product, resulting from the replacement of an α-hydrogen atom, is that expected statistically and is independent of the relative rates of protium and deuterium abstraction. This circumstance illustrates a statement previously made (Bryce-Smith, Gold, and Satchell, *loc. cit.*) emphasising the dependence of the isotopic composition of the reaction product, not only on the relative ease of abstraction and abundance of the isotopic atoms, but also on their distribution.

The proportion of deuterium found in the 4 : 4′-dimethyldibenzyl was 6·4 ± 0·1 atoms %. The atom percentages calculated on the assumptions that protium abstraction is (*a*) as probable as deuterium abstraction, (*b*) twice as probable, and (*c*) infinitely more probable are 6·49, 6·88, and 7·30, respectively. (This calculation is based on the isotopic composition of the xylene sample employed, and takes into account the small amount of nuclear deuteration.) The experimental value agrees only with the first of these assumptions. This result can, in the light of previous discussion, be interpreted in two ways. It means either that the rates of protium and deuterium abstraction are identical

* The atom percentage of deuterium represents the ratio, multiplied by 100, of the number of deuterium atoms in the compound to the *total* number of hydrogen (protium and deuterium) atoms in it.

† The fractional abundance of the species $X^2H_n{}^1H_{m-n}$, where *m* is the number of equivalent replaceable hydrogen atoms in the molecule, is given by $m!p^n(1-p)^{m-n}/n!(m-n)!$ where *p* is the fraction of deuterium atoms in the replaceable hydrogen atoms of the whole system.

or that the radicals thus formed attain, or at any rate approach, isotopic equilibrium with the solvent xylene before appreciable dimerisation occurs. In view of the experimental evidence to the contrary, the first of these alternatives seems untenable and we conclude that, under the specific conditions of our experiments, hydrogen abstraction occurs much more readily than dimerisation.

In a suitable case the validity of the assumption implicit in this view concerning the relative velocities of protium and deuterium abstraction by the initiating radical X· (phenyl or benzoyloxy-radicals in the present case) could be tested by carrying out an isotopic assay on the substance XH. The method could then be elaborated into a technique for measuring the chain length of the self-propagation reaction (iv). In the present work it was not experimentally possible to carry out an assay on the benzene or benzoic acid formed.

With the aid of a mass spectrometer, or by infra-red spectrometry, it might also be possible to observe the isotopic randomisation of deuterium among the *p*-xylene molecules produced by the chain reaction.

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Organometallic and Organometalloidal Fluorine Compounds. Part XII. Bistrifluoromethylphosphinic Acid and Related Phosphorus Oxyacids.*

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[Reprint Order No. 5637.]

Bistrifluoromethylphosphinic acid, $(CF_3)_2PO{\cdot}OH$, is conveniently prepared by hydrolysis of $(CF_3)_2PCl_3$ or $(CF_3)_2PCl_3$. It is the strongest acid of phosphorus ($K > 10^{-1}$), and conductivity measurements in acetic acid solution show it to be one of the strongest known acids: the order of decreasing strength, with approximate relative strengths shown in parentheses, is $HClO_4$ (360) > $(CF_3)_2PO{\cdot}OH$ (250) > HBr (180) > H_2SO_4 (32) > $CF_3{\cdot}PO(OH)_2$, HCl (9) > $(CF_3)_2AsO{\cdot}OH$ (3·5) > $CF_3{\cdot}AsO(OH)_2$ (2·5) > $CF_3{\cdot}CO_2H$, HNO_3, $C_3F_7{\cdot}CO_2H$ (1).

Trifluoromethylphosphonous acid disproportionates in concentrated aqueous solution to yield trifluoromethylphosphine and trifluoromethylphosphonic acid, and the anhydrous acid cannot be isolated. The phosphonous acid has weak reducing properties and is moderately strong ($K = 9{\cdot}8 \times 10^{-2}$). Infrared spectroscopic studies of the P:O bond in trifluoromethylphosphorus compounds are included.

OXIDATIVE hydrolysis of the compounds $CF_3{\cdot}PX_2$ or $(CF_3)_2PX$ (X = Cl or I), or controlled hydrolysis of tristrifluoromethylphosphine followed by oxidation, yields the white crystalline trifluoromethylphosphonic acid, $CF_3{\cdot}PO(OH)_2$, which is strong and dibasic (Part X, Bennett, Emeléus, and Haszeldine, *J.*, 1954, 3598). A second acid, trifluoromethylphosphonous acid, $CF_3{\cdot}P(OH)_2$, is also obtained in solution by the aqueous hydrolysis of compounds of the type $CF_3{\cdot}PX_2$ or $(CF_3)_2PX$; this acid is volatile with water vapour at low pressures, is monobasic, and yields a sodium salt whose infrared spectrum shows its structure to be $CF_3{\cdot}PH(:O)(ONa)$ rather than $CF_3{\cdot}P(OH)(ONa)$. The present communication describes the preparation and characterisation of a further acid, bistrifluoromethylphosphinic acid, $(CF_3)_2PO{\cdot}OH$, and also experiments which serve to characterise more fully

* Part XI, Bennett, Emeléus, and Haszeldine, *J.*, 1954, 3896.

trifluoromethyl-phosphonous and -phosphonic acids, and to establish their inter-relationship.

By analogy with trifluoromethyl-phosphonous and -phosphonic acids, one route to bistrifluoromethylphosphinic acid would be by oxidation of bistrifluoromethylphosphinous acid, but earlier studies (Parts X, XI, *locc. cit.*) have shown that the last acid is unstable in aqueous solution and decomposes to yield fluoroform and trifluoromethylphosphonous acid, *e.g.*,

$$(CF_3)_2PI \xrightarrow{H_2O} (CF_3)_2P{\cdot}OH \xrightarrow{H_2O} CHF_3 + CF_3{\cdot}P(OH)_2$$

This is in marked contrast to the hydrolysis of dialkylmonohalogenophosphines which yields the dialkylphosphinic acid and the dialkylphosphine (Dorken, *Ber.*, **1888**, **21**, 1505; Michaelis and Gleichmann, *Ber.*, 1882, **15**, 801):

$$2R_2PX + 2H_2O \longrightarrow R_2PH + R_2PO(OH) + 2HX$$

A dialkylphosphinous acid has not yet been reported. An alternative route to bistrifluoromethylphosphinic acid was sought and found in the hydrolysis of bistrifluoromethylphosphorus trichloride:

$$(CF_3)_2PI \xrightarrow{AgCl} (CF_3)_2PCl \xrightarrow{Cl_2} (CF_3)_2PCl_3 \xrightarrow{H_2O} (CF_3)_2PO{\cdot}OH$$

The reaction of chlorine with chlorobistrifluoromethylphosphine is exothermic and is best effected in the liquid phase at low temperature. The trichloride (b. p. *ca.* 107°) is less volatile than tristrifluoromethylphosphorus dichloride (b. p. 80°; Part VII, Bennett, Emeléus, and Haszeldine, *J.*, 1953, 1565). Evaporation of its hydrolysate to dryness leaves no residue, thus showing that bistrifluoromethylphosphinic acid is volatile in water vapour like trifluoromethylphosphonous acid. The acid was isolated by formation of its water-soluble silver salt, which could be recrystallised from organic solvents. When heated under reduced pressure with concentrated sulphuric acid, the silver salt yielded a distillate of the viscous, colourless, bistrifluoromethylphosphinic acid. The acid is stable to distillation at atmospheric pressure (b. p. 182°/760 mm.), fumes in air, and is a strong monobasic acid. By contrast, dimethylphosphinic acid (m. p. 87°) is a very weak acid (Kabachinik and Shepeleva, *Izvest. Akad. Nauk, S.S.S.R., Otdel Khim. Nauk*, 1949, **1**, 56; *Chem. Abs.*, 1949, **43**, 5739; Crofts and Kosolapoff, *J. Amer. Chem. Soc.*, 1953, **75**, 3381). Only one mole of fluoroform per mole of acid is liberated by reaction of bistrifluoromethylphosphinic acid with an excess of aqueous sodium hydroxide, since the alkali-stable trifluoromethylphosphonic acid is produced:

$$(CF_3)_2PO{\cdot}ONa \xrightarrow{NaOH} CF_3{\cdot}PO(ONa)_2 + CHF_3$$

Loss of fluoroform begins at pH $> 8{\cdot}7$.

A more convenient synthesis of bistrifluoromethylphosphinic acid utilises the readily-accessible tristrifluoromethylphosphine, which reacts smoothly with chlorine to give tristrifluoromethylphosphorus dichloride (Part VII, *loc. cit.*). Aqueous hydrolysis of the last compound occurs quantitatively according to the equation

$$(CF_3)_2PCl_3 \xrightarrow{H_2O} [(CF_3)_2P(OH)_3] \longrightarrow (CF_3)_2PO{\cdot}OH + CHF_3$$

The expected instability of the intermediate $(CF_3)_2P(OH)_3$ is confirmed by the fact that tristrifluoromethylphosphine oxide, prepared by reaction of tristrifluoromethylphosphorus dichloride with anhydrous oxalic acid, yields bistrifluoromethylphosphinic acid when treated with water (Paul, following note). The difference between trifluoromethyl compounds and alkyl or aryl compounds is illustrated by the hydrolysis of R_3PX_2 (R = alkyl or aryl, X = halogen or pseudo-halogen), which yields phosphine oxides which are stable in water and form stable hydrates (*e.g.*, Steinkopf, Buckhein, and Krasser, *Ber.*, 1921, **54**, 1024; Michaelis and Soden, *Annalen*, 1885, **229**, 306). Bistrifluoromethylphosphinic acid readily yields a crystalline aniline salt which, since it decomposes when heated, is best characterised

by means of its infrared spectrum (C.S. No. 142).* The salt shows an acid reaction in aqueous solution (pH *ca.* 3), and can be titrated with aqueous sodium hydroxide.

Hydrolysis of tristrifluoromethylphosphorus dichloride with aqueous base yields trifluoromethylphosphonic acid together with two molecular proportions of fluoroform :

$$(CF_3)_3PCl_2 \xrightarrow{NaOH} CF_3{\cdot}PO(ONa)_2 + 2CHF_3$$

This forms a convenient method for the preparation of trifluoromethylphosphonic acid and is an alternative to the several routes described earlier (Parts X and XI, *locc. cit.*). The preparation of the acid from the iodo-compounds $CF_3{\cdot}PI_2$ and $(CF_3)_2PI$ has been used on a larger scale than hitherto, and is somewhat more convenient than the preparation from tristrifluoromethylphosphine, since the iodo-compounds can be manipulated in conventional apparatus. Trifluoromethylphosphonic acid has been further characterised by formation of its mono- and di-potassium salts, and its mono- and di-aniline salts. The aniline salts are particularly useful, since they can be recrystallised from organic solvents, give well-defined infrared spectra (C.S. Nos. 143 and 144), and can be titrated with aqueous base. The P:O stretching vibration in the infrared for anilinium bistrifluoromethylphosphinate 7·85 μ) and mono- (7·97 μ) and di-anilinium trifluoromethylphosphonate (8·06 μ) can be assigned with less certainty than that for the other trifluoromethyl derivatives (see Table 3), since other strong bands appear in the 7·7—8·2 μ region. The assignment for the trifluoromethylphosphonic acid salts is supported by the fact that the shift in P:O vibration from the mono- to the di-salt is similar to that observed for the mono- and di-sodium and -potassium salts (Table 1). The N–H stretching vibration in the infrared spectrum of the aniline salts moves from the usual region near 3·0 μ to the amine-salt region at longer wavelength [anilinium bistrifluoromethylphosphinate, 3·76, 4·74 ; monoanilinium trifluoromethylphosphonate, 3·80, 4·75 ; dianilinium trifluoromethylphosphonate, 3·85, 4·63 μ].

A continuation of the study of trifluoromethylphosphonous acid has revealed the general properties of this acid and its relationship to other trifluoromethyl phosphorus oxy-acids. In applying the original preparation of trifluoromethylphosphonous acid (Parts X and XI, *locc. cit.*), on a larger scale, vigorous shaking of tristrifluoromethylphosphine with one equivalent of aqueous base is needed to bring about a rapid reaction and prevent hydrolysis of trifluoromethylphosphonous acid by the base which has not reacted :

$$(CF_3)_3P + OH^- \longrightarrow (CF_3)_2PO^- + CHF_3$$
$$(CF_3)_2PO^- + H_2O \longrightarrow CF_3{\cdot}PHO(O^-) + CHF_3$$
$$CF_3{\cdot}PHO(O^-) + OH^- \longrightarrow HPO_3^{--} + CHF_3$$

Trifluoromethylphosphonous acid has been further characterised as its potassium salt. Aqueous solutions of the free acid are obtained by distillation of the alkali-metal salts with dilute sulphuric acid; since fluoroform is liberated from the acid only at pH > 11, the concentration of aqueous solutions of trifluoromethylphosphonous acid can be determined by titration with carbonate-free aqueous alkali. The reducing properties of the acid were studied : it is not oxidised by iodine solution in presence of sodium hydrogen carbonate (cf. phosphorous acid which is oxidised quantitatively under these conditions) ; saturated mercuric chloride solution gave no immediate precipitate at room temperature (cf. the immediate precipitate with phosphorous acid), but a slow reaction occurred at 60° according to the equation

$$CF_3{\cdot}PHO(OH) + 2HgCl_2 + H_2O \longrightarrow CF_3{\cdot}PO(OH)_2 + Hg_2Cl_2 + 2HCl$$

Oxidation of trifluoromethylphosphonous acid by ceric sulphate, potassium iodate, or potassium dichromate solution is slow and is not quite complete after several hours at room temperature; oxidation by acidified potassium permanganate solution at 60° is more rapid and essentially quantitative. These results show that replacement of hydrogen in phosphorous acid by a perfluoroalkyl group considerably lessens the reducing power, but increases the acid strength (see below).

Trifluoromethylphosphonous acid is quantitatively hydrolysed to fluoroform and phos-

* Infrared spectra thus recorded have been deposited with the Society. Photocopies may be obtained, price 3*s.* 0*d.* per copy, on application to the General Secretary.

phorous acid when its aqueous solution is heated at 100°. In more concentrated aqueous solution, trifluoromethylphosphonous acid prepared from di-iodotrifluoromethylphosphine similarly yields fluoroform and an equivalent of phosphorous acid when heated at 140°;

$$[CF_3{\cdot}P(OH)_2 \xrightarrow{H_2O} CHF_3 + H_3PO_3]$$

an independent side-reaction (8% of the total reaction) produces trifluoromethylphosphine and trifluoromethylphosphonic acid:

$$3CF_3{\cdot}P(OH)_2 \longrightarrow CF_3{\cdot}PH_2 + 2CF_3{\cdot}PO(OH)_2$$

This disproportionation of trifluoromethylphosphonous acid also occurs at room temperature, and its relative importance depends mainly upon the concentration of the acid solution. Thus, when di-iodotrifluoromethylphosphine is hydrolysed by the minimum amount of water, to give a very concentrated solution of trifluoromethylphosphonous acid, evaporation of the solution *in vacuo* leaves a white crystalline dibasic acid and trifluoromethylphosphine is produced (Parts VII, XI, *locc. cit.*). The dibasic acid has now been identified as trifluoromethylphosphonic acid by preparation of its mono- and dipotassium salts and mono- and di-aniline salts, and comparison of their infrared spectra with those of authentic samples. The molar ratio of trifluoromethylphosphine to trifluoromethylphosphonic acid is as expected from the last equation. The hydrolysis of di-iodotrifluoromethylphosphine has been studied with varying amounts of water, and when the trifluoromethylphosphonous acid is produced in relatively dilute solution, it is completely volatile in water vapour when evaporated to dryness *in vacuo*, *i.e.*, the disproportionation reaction does not occur. Trifluoromethylphosphonous acid prepared from other sources [*e.g.*, hydrolysis of $(CF_3)_2PI$ or $CF_3{\cdot}PCl_2$] shows similar behaviour.

Disproportionation to trifluoromethylphosphine also occurred during unsuccessful attempts to prepare anhydrous trifluoromethylphosphonous acid by reaction of potassium trifluoromethylphosphonite with phosphoric acid and phosphoric anhydride (cf. preparation of bistrifluoromethylphosphinic acid), and it must be concluded that anhydrous trifluoromethylphosphonous acid cannot be prepared by reactions of this type. This is in accord with the properties of alkyl- and aryl-phosphonous acids; *e.g.*, phenyl-, *iso*amyl-, and ethylphosphonous acids disproportionate according to the equation $3R{\cdot}P(OH)_2 \longrightarrow R{\cdot}PH_2 + 2R{\cdot}PO(OH)_2$ and even phosphorous acid, the parent acid, reacts as $4H_3PO_3 \longrightarrow 3H_3PO_4 + PH_3$ when heated (Ananoff, *Ber.*, 1875, **8**, 499; Goddard, in Newton Friend's "Textbook of Inorganic Chemistry," Griffin and Co., London, 1936, XI, p. 32; Vigier, *Bull. Soc. chim. France*, 1869, **11**, 125).

The tentative assignments for the P:O ($P^+–O^-$) stretching vibration in the infrared made in Part X for certain trifluoromethylphosphorus compounds are strongly supported by the spectra of the compounds prepared during the present work. The data in Table 1 show the assignments made for P:O (stretching), C–F (stretching), PO–H (stretching), POH (deformation), and CF_3 (deformation).

A movement of the P:O ($P^+–O^-$) bond stretching vibration to shorter wave-lengths can be correlated with an increase in its force constant, in its double-bond character, and in the strength of the corresponding oxy-acid. Such a movement is brought about by presence of electronegative groups on the phosphorus atom, as can be seen from Table 1, and particularly by comparison of the P:O bands for derivatives of trifluoromethylphosphonic acid (*ca.* 8·0 μ) with the derivatives of the stronger bistrifluoromethylphosphinic acid (*ca.* 7·8 μ). Corresponding shifts to shorter wave-length of the carbonyl frequency in fluorocarboxylic acids and their derivatives have been noted (*e.g.*, $CH_3{\cdot}CO_2H$ 5·85 μ, $CF_3{\cdot}CO_2H$ 5·60 μ; Haszeldine, *Nature*, 1951, **168**, 1028). The P:O vibration in the series POF_3, $(CF_3)_3PO$, $POCl_3$ gives, to a first approximation, a measure of the negativity of the CF_3 group. When three fluorine atoms are attached to the phosphorus, the P:O vibration is at the shortest wave-length (7·07 μ); a CF_3 group is less negative than fluorine, but apparently more electron-attracting than chlorine, since the P:O vibration in the phosphine oxide appears at 7·53 μ. Intermediate values can be expected for compounds such as $CF_3{\cdot}POF_2$, $(CF_3)_2POF$, $CF_3{\cdot}POCl_2$, and $(CF_3)_2POCl$.

Relative Strengths of Trifluoromethyl Oxy-acids.—It has been shown by conductivity

measurements (Part VIII, *loc. cit.*) that trifluoromethylarsonic acid and bistrifluoromethylarsinic acid are almost completely ionised in water, and that in anhydrous acetic acid as solvent the order of acid strength, compared with that of other strong acids, is

TABLE 1. *The* P:O *stretching vibration.*

	C.S. No.	P:O	Other assignments
$CF_3{\cdot}PO(OK)(OH)$	145	7·93	PO–H 4·3; POH deformation 10·57; CF_3 13·50; C–F 8·32, 8·95
$CF_3{\cdot}PO(OK)_2$	146	8·07	C–F 8·7; CF_3 13·65; no POH bands
$CF_3{\cdot}PO(ONa)(OH)$ [a]	— [b]	7·99	PO–H 4·25; CF_3 13·5; C–F 8·35
$CF_3{\cdot}PO(ONa)_2$ [a]	—	8·05	CF_3 13·6; C–F 8·50, 8·75; no POH bands
$CF_3{\cdot}PO(OH)_2$	—	8·0—8·1	C–F 8·69, 8·83; CF_3 13·15
$CF_3{\cdot}PH(:O)(ONa)$ [a]	—	8·05	P–H 4·2; CF_3 13·6; C–F 8·80, 9·00
$(CF_3)_2PO{\cdot}OH$	147	7·80	PO–H 4·25; CF_3 13·34; C–F 8·3, 8·5, 8·74
$(CF_3)_2PO(OAg)$	148	7·84	C–F 8·10, 8·23, 8·67; CF_3, 13·43; no POH bands
$Ph{\cdot}NH_3{}^+(CF_3)_2PO{\cdot}O^-$	142	7·85	C–F 8·65, 8·73
$Ph{\cdot}NH_3{}^+CF_3{\cdot}PO(OH){\cdot}O^-$	143	7·97	C–F 8·6, 8·95
$(Ph{\cdot}NH_3{}^+)_2CF_3{\cdot}PO(O^-)_2$	144	8·06	C–F 9·03
$(CF_3)_2PO$ [c]	—	7·53	C–F 8·27, 8·45; CF_3 13·36
$POCl_3$ [d]	—	7·70	
POF_3 [d]	—	7·07	

[a] Parts X and XI, *locc. cit.* [b] Paul, *J.*, 1954, following note. [c] Meyrick and Thompson, *J.*, 1950, 225, report P:O 7·81 μ. [d] Gutowsky and Liehr, *J. Chem. Phys.*, 1952, **20**, 1652.

$H_2SO_4 > HCl > (CF_3)_2AsO(OH) > CF_3{\cdot}As(OH)_2 \gg CF_3{\cdot}CO_2H$, HNO_3, $C_3F_7{\cdot}CO_2H$. These observations have now been extended by measurements on aqueous solutions of trifluoromethylphosphonic, bistrifluoromethylphosphinic, and trifluoromethylphosphonous acids, and by measurements on the first two of these in acetic acid solution.

Bistrifluoromethylphosphinic acid and trifluoromethylphosphonous acid are monobasic, and the graphs of molecular conductivity against square-root of concentration, which are straight lines at low concentrations, lead to values for equivalent conductivity at infinite dilution of 385·7 and 379·0 respectively (see Tables 6 and 7). The graph for trifluoromethylphosphonous acid becomes a curve at higher concentrations (see Table 7). The ionic conductivities of $(CF_3)_2PO{\cdot}O^-$ and $CF_3{\cdot}PHO(O^-)$ calculated from the data are 35·9 and 29·1 respectively [cf. $(CF_3)_2AsO{\cdot}O^-$, 49·6; $CF_3{\cdot}AsO(OH){\cdot}O^-$, 48·1]. The degree of ionisation (α) of bistrifluoromethylphosphinic and trifluoromethylphosphonous acids in aqueous solution as a function of concentration is shown in Table 2.

TABLE 2.*

		$CF_3{\cdot}P(OH)_2$			$(CF_3)_2PO(OH)$		
c	$\sqrt{c}$	λ_v	λ_e	α	λ_v	λ_e	α
0·020	0·1415	349·7	358·5	0·975	365·1	364·7	1·002
0·010	0·1000	354·7	364·5	0·973	371·2	370·9	1·002
0·002	0·0447	366·5	372·5	0·984	379·3	379·0	1·001
0·001	0·0316	370·9	374·4	0·990	381·3	381·0	1·000

* For meaning of c, λ_v, and λ_e see p. 573.

Potentiometric titration gave $K_1 = 6{\cdot}8 \times 10^{-2}$, $K_2 = 1{\cdot}2 \times 10^{-4}$ for trifluoromethylphosphonic acid in aqueous solution (Part X, *loc. cit.*). Examination of the conductivity of aqueous solutions of the acid shows that the graph of molecular conductivity against the square-root of concentration is a smooth curve, even at low concentrations. Since λ_e is high (see Table 5) it follows that one hydrogen atom in the phosphonic acid is almost completely ionised, and the extent of ionisation of the second hydrogen atom increases with dilution. This behaviour is consistent with the relatively small ratio of the dissociation constants (*ca.* 575, Part X), and in this respect the acid resembles sulphuric, oxalic, and malonic acids, which also do not give straight lines for λ_e–$\sqrt{c}$ plots, and have a small $K_1 : K_2$ ratio. The conductivities of aqueous solutions of mono- and di-potassium trifluoromethylphosphonates have also been studied and the results are shown in Tables 8 and 9. The λ_e–$\sqrt{c}$ plot for the monopotassium salt clearly shows the gradual ionisation of the one ionisable hydrogen atom present in the molecule, since a distinct smooth curve is obtained. A similar plot for the dipotassium salt gives a shallow curve which shows an

almost linear relationship at low concentration; the equivalent conductivity at infinite dilution is 256, whence the ionic conductivity for $\frac{1}{2}[CF_3 \cdot PO_3^{--}]$ is 53·5.

Very approximate values for the ionisation constants of bistrifluoromethylphosphinic and trifluoromethylphosphonous acids, obtained by application of the equation $K =$

FIG. 1.

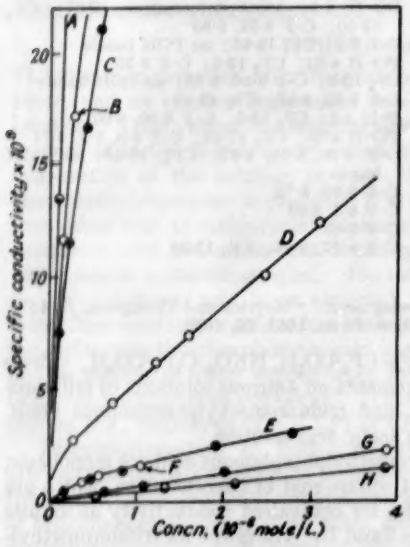


FIG. 2.

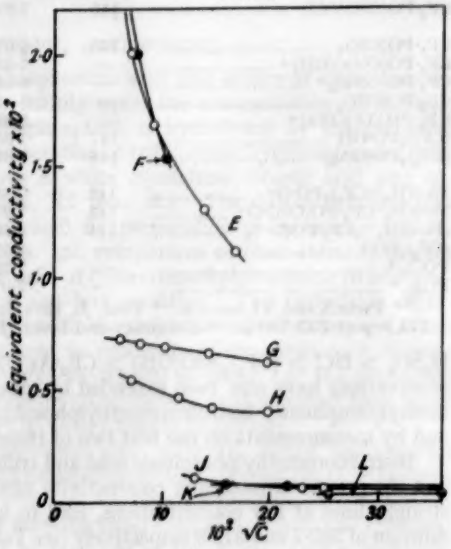
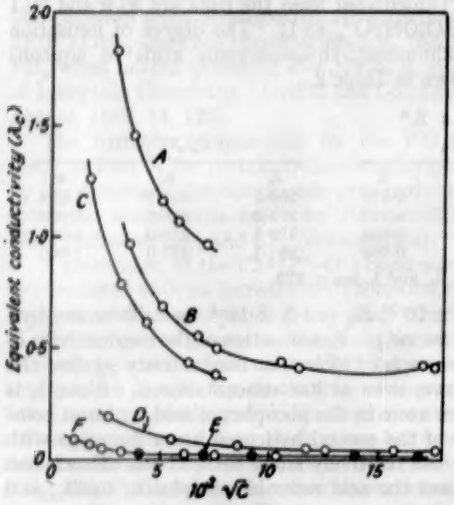


FIG. 3.



Conductivities in acetic acid.

A, $HClO_4$.
B, $(CF_3)_2PO \cdot OH$.
C, HBr.
D, H_2SO_4.
E, $CF_3 \cdot PO(OH)_2$.
F, HCl.
G, $(CF_3)_2AsO \cdot OH$.
H, $CF_3 \cdot AsO(OH)_2$.
J, HNO_3.
K, $CF_3 \cdot CO_2H$.
L, $C_3F_7CO_2H$.

$c\alpha^2/(1 - \alpha)$, enable a comparison of phosphorus and arsenic acids to be made (Table 3), and again reveal the marked increase in acid strength when alkyl are replaced by perfluoroalkyl groups.

In view of the well-known inaccuracies involved in calculating K from values of α for strong acids, the relative strengths of the trifluoromethyl phosphorus and arsenic acids cannot be compared accurately from the data in Table 3. Determination of the con-

ductivities of trifluoromethylphosphonic and bistrifluoromethylphosphinic acid in acetic acid solution (Tables 10 and 11) enables this comparison to be made, however. The failure to isolate anhydrous trifluoromethylphosphonous acid prevented an investigation of its strength in acetic acid solution. The specific conductivities of the acids studied in this

TABLE 3.

$CF_3 \cdot PO(OH)_2$	K_1 6·8 × 10^{-3} K_2 1·2 × 10^{-4}	$CH_3 \cdot PO(OH)_2$	K_1 4·2 × 10^{-3} K_2 1·8 × 10^{-8}	H_3PO_4	K_1 7·5 × 10^{-3} K_2 6·2 × 10^{-8} K_3 1·1 × 10^{-12}
$(CF_3)_2PO \cdot OH$	$K > 10^{-1}$	$(CH_3)_2PO \cdot OH$	K 8·3 × 10^{-4}		
$CF_3 \cdot P(OH)_2$	K 9·8 × 10^{-3}	$CH_3 \cdot P(OH)_2$	—	H_3PO_3	K_1 1 × 10^{-2} K_2 2 × 10^{-7}
$CF_3 \cdot AsO(OH)_2$	K_1 7·5 × 10^{-3} K_2 3 × 10^{-6}	$CH_3 \cdot AsO(OH)_2$	K_1 2·5 × 10^{-4} K_2 5·7 × 10^{-9}	H_3AsO_4	K_1 5 × 10^{-3} K_2 4 × 10^{-8} K_3 6 × 10^{-10}
$(CF_3)_2AsO \cdot OH$	K 3·8 × 10^{-3}	$(CH_3)_2AsO \cdot OH$	K_a 7·5 × 10^{-7} K_b 5·6 × 10^{-12}		

way vary from about 1 × 10^{-3} for heptafluorobutyric acid (Part IX, *loc. cit.*) to 2600 × 10^{-3} for bistrifluoromethylphosphinic acid. The results plotted as specific conductivity against concentration (Fig. 1) give a general picture of relative acid strengths with $HClO_4 > (CF_3)_2PO(OH) > HBr > H_2SO_4 > CF_3 \cdot PO(OH)_2$, $HCl > (CF_3)_2AsO \cdot OH > CF_3 \cdot AsO(OH)_2 > CF_3 \cdot CO_2H$, HNO_3, $C_3F_7 \cdot CO_2H$. Acids which are weak in acetic acid solution (HNO_3, $CF_3 \cdot CO_2H$, $C_3F_7 \cdot CO_2H$) cannot be plotted conveniently in this way, and are better compared by use of a plot of equivalent conductivity against square root of concentration (Figs. 2 and 3). The curve for bistrifluoromethylphosphinic acid (Fig. 3) shows a minimum, and similar minima have been noted by Hlasko and Michalski (*Roczn. Chem.*, 1938, **18**, 220) for hydrochloric, hydrobromic, and hydriodic acids. If the values of equivalent conductivity at a particular concentration ($c = 0{\cdot}49$; $10\sqrt{c} = 7$) are taken as a qualitative measure of the extent of ionisation (it being assumed that the anionic conductivities are approximately equal), the relative strengths of the acids, with $CF_3 \cdot CO_2H$, HNO_3, and $C_3F_7 \cdot CO_2H$ being taken as unity, are shown in Table 4.

TABLE 4. *Relative strengths of acids.*

$HClO_4$	360	$CF_3 \cdot PO(OH)_2$	9	$CF_3 \cdot CO_2H$	1
$(CF_3)_2PO(OH)$	250	HCl		HNO_3	
HBr	180	$(CF_3)_2AsO \cdot OH$	3·5	$C_3F_7 \cdot CO_2H$	
H_2SO_4	32	$CF_3 \cdot AsO(OH)_2$	2·5		

The difference between trifluoromethylarsonic acid and bistrifluoromethylarsinic acid (Part IX, *loc. cit.*) is much less than that between the corresponding phosphorus acids (Fig. 1). Bistrifluoromethylphosphinic acid is the strongest acid of phosphorus and, as shown in Fig. 1, is one of the strongest known acids.

EXPERIMENTAL

The general techniques used were the same as described in earlier papers.

Bistrifluoromethylphosphinic Acid.—(a) *Bistrifluoromethylphosphorus trichloride.* Chlorobistrifluoromethylphosphine (13·4 g., 0·065 mole; prepared as described in Part VII) and a deficit of chlorine (4·0 g., 0·056 mole) in a sealed tube were warmed slowly from −80° to room temperature. The vigorous exothermic reaction was controlled by external cooling. After being kept for 48 hr., the products were distilled initially *in vacuo* and without contact with mercury, finally in a conventional distillation apparatus in an atmosphere of nitrogen, to give *bistrifluoromethylphosphorus trichloride* (13·8 g., 75%), b. p. 82°/355 mm. (Found: Cl, 38·1. $C_2Cl_3F_6P$ requires Cl, 38·6%). Its b. p., calculated by extrapolation of the vapour-pressure curve measured over a short temperature range, is *ca.* 107°/760 mm. The colourless liquid fumes slightly in air and has an odour like that of phosphorus pentachloride. Reaction of bistrifluoromethylphosphorus trichloride (0·2607 g.) with an excess of 15% aqueous sodium hydroxide (10 ml.) for 48 hr. gave fluoroform (0·066 g.); this corresponds to the loss of one trifluoromethyl group as fluoroform (Found: CF_3, 25·0. $C_2Cl_3F_6P$ requires CF_3, 50·1%). The infrared spectrum of bistrifluoromethylphosphorus trichloride (C.S. No. 149) shows strong C–F stretching vibrations at 8·47 and 8·73 μ.

(b) *Silver bistrifluoromethylphosphinate.* Bistrifluoromethylphosphorus trichloride (1·61 g.) and water (5 ml.) reacted immediately, and after 12 hr., examination of the volatile material showed that fluoroform was absent. Freeze-drying of the aqueous solution left no residue,

showing that the product is volatile in water vapour. Silver oxide (5 g.) was added slowly to the stirred condensate and after 12 hr. the solution was filtered from silver chloride and the excess of oxide. Freeze-drying of the solution gave a white solid which was dried (P_2O_5) *in vacuo* for 24 hr. then recrystallised from carbon tetrachloride–ether to give *silver bistrifluoromethylphosphinate* (1·7 g., 95%) [Found: CF_3 (as fluoroform), 22·6; Ag, 35·2. $C_2O_2F_6PAg$ requires CF_3, 44·7; Ag, 35·0%]. Silver was determined as silver chloride and CF_3 as fluoroform by hydrolysis with an excess of aqueous sodium hydroxide; only one of the two CF_3 groups is removed under these conditions.

(c) *Isolation of bistrifluoromethylphosphinic acid.* Silver bistrifluoromethylphosphinate (9·0 g.) and concentrated sulphuric acid (5 ml.) were mixed in the bulb of a distillation apparatus and slowly heated in a nitrogen atmosphere. Two layers were formed: the lower was a solution of silver sulphate in sulphuric acid, and the upper layer distilled on rise of temperature to give *bistrifluoromethylphosphinic acid* (5·6 g., 95%), b. p. 137—138°/238 mm., 182°/760 mm. [Found: CF_3 (as fluoroform), 33·9%; equiv., 205. $C_2HO_2F_6P$ requires CF_3, 68·3%; equiv., 202]. Only one of the CF_3 groups was lost as fluoroform on hydrolysis with 15% aqueous sodium hydroxide. The equivalent weight was determined by pH titration of 0·01M-acid (10·0 ml.) against 0·1N-sodium hydroxide solution. The point of inflection was *ca.* pH 6·5, and above pH 8·7 decomposition with liberation of fluoroform and a decrease in pH became apparent.

(d) *Anilinium bistrifluoromethylphosphinate.* To the acid (0·29 g.), dissolved in water (2·5 ml.), was added aniline (0·15 g.), and the mixture was boiled to give a clear solution which deposited crystals on cooling. Recrystallisation from benzene gave *anilinium bistrifluoromethylphosphinate* (0·22 g.) (Found: C, 32·8; H, 3·1; N, 4·8%; equiv., 297. $C_8H_9O_2NF_6P$ requires C, 32·6; H, 2·7; N, 4·8%; equiv., 295). The equivalent weight was determined by direct titration with 0·0878N-sodium hydroxide solution.

(e) *Preparation from tristrifluoromethylphosphorus dichloride.* The chloro-compound was prepared by the method described in Part VII. Tristrifluoromethylphosphorus dichloride (1·235 g.) and water (3 ml.) underwent an exothermic reaction to give, after 48 hr., fluoroform (0·272 g., 33%) and an aqueous solution which was completely volatile when subjected to the freeze-drying procedure. The condensate was treated with an excess of freshly-prepared silver oxide (3 g.) and after 6 hr. was filtered and freeze-dried to give silver bistrifluoromethylphosphinate (1·18 g., 95%) (Found: Ag, 35·1. Calc. for $C_2O_2F_6PAg$: Ag, 35·0%) identified by means of its infrared spectrum.

Reaction of tristrifluoromethylphosphorus dichloride (0·340 g.) with 10% aqueous sodium hydroxide (10 ml.) for 48 hr. gave fluoroform (0·154 g., 67%) and an aqueous solution which, when freeze-dried, left a residue of disodium trifluoromethylphosphonate, identified by means of its infrared spectrum.

Trifluoromethylphosphonic Acid.—(a) *Potassium salts.* Trifluoromethylphosphonic acid (4·105 g.), purified by sublimation *in vacuo* and dried *in vacuo* (over P_2O_5) for 6 hr., was dissolved in water (20 ml.) and neutralised with 5% potassium carbonate solution (3·78 g. of K_2CO_3 required). A pH meter accurate to $\pm$0·02 unit was used to determine the end-point. The solution was freeze-dried (2 days) to give *dipotassium trifluoromethylphosphonate* (6·1 g., 97%) (Found: K, 34·6. $CO_3F_3K_2P$ requires K, 34·5%).

Trifluoromethylphosphonic acid (1·067 g.) was dissolved in water (20 ml.) and a solution of potassium carbonate (0·4917 g.) in water (10 ml.) was added with stirring. Freeze-drying (24 hr.) gave *monopotassium trifluoromethylphosphonate* (1·297 g., 95%) (Found: K, 20·8. CHO_3F_3KP requires K, 20·8%).

(b) *Aniline salts.* Aniline (0·17 g.), dissolved in ethanol (1 ml.), was slowly added to trifluoromethylphosphonic acid (0·29 g.). The mixture was heated (100°) until solution was complete, and after cooling, *monoanilinium trifluoromethylphosphonate* (0·3 g.) (Found: C, 34·1; H, 4·0; N, 5·5. $C_7H_9O_3NF_3P$ requires C, 34·5; H, 3·7; N, 5·7%) was removed by filtration and recrystallised from ethanol.

Similar reaction of aniline (0·45 g.), ethanol (2 ml.), and trifluoromethylphosphonic acid (0·36 g.) gave *dianilinium trifluoromethylphosphonate* (0·5 g.) (Found: C, 46·2; H, 5·3; N, 8·6. $C_{13}H_{16}O_3N_2F_3P$ requires C, 46·4; H, 4·8; N, 8·3%), recrystallised from ethanol.

The aniline salts decomposed without melting when heated, and were therefore characterised by their infrared spectra.

(c) *Preparation.* The method described in Part X was used, with the improvement that the crude mixture of iodobistrifluoromethylphosphine and di-iodotrifluoromethylphosphine obtained by distillation of the reaction products of trifluoroiodomethane and phosphorus was used directly. In a typical experiment, the mixture (20 g.) was added to water (50 ml.), and the two phases were

stirred for 2 hr. During this period the two layers became homogeneous and fluoroform was liberated during the exothermic reaction. When cold, the solution was treated with unstabilised 100-vol. hydrogen peroxide, added dropwise with constant stirring until iodine was no longer liberated and the exothermic reaction ceased. After filtration, the solution was freeze-dried (4 days) to give crude trifluoromethylphosphonic acid, which was purified by sublimation (6·1 g.) (Found : equiv., 75·4. Calc. for $CH_2O_3F_3P$: equiv., 75·0). Since the acid is very hygroscopic it was manipulated in a dry box and was dried *in vacuo* for 6 hr. before use.

Trifluoromethylphosphonous Acid.—(a) *Potassium salt.* Tristrifluoromethylphosphine (4·5 g., 0·019 mole) and 0·147N-aqueous potassium hydroxide (100 ml., 0·015 mole) in a 250-ml. Carius tube were shaken vigorously in a vibro-shaker for 24 hr. Fluoroform and unreacted tristrifluoromethylphosphine (21%) were removed, and the residual aqueous solution was freeze-dried (48 hr.) to give *potassium trifluoromethylphosphonite* (2·5 g., 98%) (Found : K, 22·9; CF_3, 40·0. CHO_2F_3KP requires K, 22·8; CF_3, 40·1%). Vigorous shaking is essential, since without rapid hydrolysis some of the potassium trifluoromethylphosphonite is hydrolysed to fluoroform by the excess of potassium hydroxide present in the early stages of the reaction, and potassium phosphite contaminates the product. Potassium was determined as chloroplatinate after a preliminary evaporation of the salt to dryness with nitric acid to prevent the reduction of the chloroplatinic acid, and CF_3 was determined as fluoroform by reaction with an excess of aqueous sodium hydroxide.

(b) *Aqueous solutions of the acid.* The method described in Part X was applied on a larger scale. In a typical experiment, tristrifluoromethylphosphine (6·0 g., 0·025 mole) and 1·011N-sodium hydroxide solution (24·9 ml., 0·025 mole) were shaken in a 150-ml. sealed tube for 48 hr. Fractionation of the volatile products gave fluoroform (3·5 g., 0·05 mole, 67%). Sulphuric acid (1 ml.) was added to the aqueous solution, and the acidic solution was freeze-dried. The condensate was again freeze-dried to remove final traces of sodium sulphate, diluted to 250 ml., and standardised by titration with carbonate-free sodium hydroxide solution.

Slighly impure solutions of trifluoromethylphosphonous acid were prepared by aqueous hydrolysis of di-iodotrifluoromethylphosphine followed by the addition of sufficient sodium carbonate to neutralise the hydriodic acid present, and freeze-drying. The distillate was aqueous trifluoromethylphosphonous acid contaminated by a small amount of iodide. In a typical experiment di-iodotrifluoromethylphosphine (2·6 g.) and water (5 ml.) were kept until the solution became homogeneous (2 hr.). Potassium carbonate (1·05 g.) was added and the solution freeze-dried to leave a residue of potassium iodide and give a distillate of trifluoromethylphosphonous acid containing a small amount of hydriodic acid.

(c) *Reducing properties of trifluoromethylphosphonous acid.* An aqueous solution of this acid, prepared from pure potassium salt as described above, was 0·0655N as determined by titration with 0·113N-sodium hydroxide with use of a pH meter to determine the end-point. Its reducing power was tested as follows :

(i) With iodine solution. Trifluoromethylphosphonous acid (10 ml. of 0·0655N) was made slightly alkaline by adding sodium hydrogen carbonate (1 g.) and kept at room temperature with 0·12N-iodine solution (20 ml.) for 18 hr. Back-titration with 0·1N-sodium thiosulphate solution (23·9 ml.) showed that no reaction had taken place.

(ii) With mercuric chloride. A solution of the acid (20 ml.) was buffered with sodium acetate (2 g.) and glacial acetic acid (2 ml.), and to it was added saturated mercuric chloride solution (20 ml.). Mercurous chloride was not produced at room temperature, but was deposited at 60°; the reaction was 93% complete after 4 hr.

(iii) With potassium iodate. A solution of the acid (10 ml.), 0·2213N-potassium iodate (30 ml.), and 5N-sulphuric acid (5 ml.) was kept overnight. Addition of an excess of potassium iodide (2 g.) and titration with 0·1235N-sodium thiosulphate solution (10·25 ml.) showed that 97% of the trifluoromethylphosphonous acid had been oxidised.

(iv) With ceric sulphate. Trifluoromethylphosphonous acid (10 ml. of 0·0655N) did not react during 5 min. at 20° with an excess of 0·1465N-ceric sulphate solution (20 ml.), but after being kept at 50° for 5 min., and left to cool (2 hr.), back-titration with 0·0901N-ferrous sulphate solution (19·7 ml.) (ferrous phenanthroline as indicator) showed that 89% had been oxidised to trifluoromethylphosphonic acid. A similar mixture, kept overnight at 20°, warmed to 50° (5 min.), cooled (2 hr.), then titrated, required 19·2 ml. of the ferrous sulphate solution, indicating that 92% of the acid had been oxidised.

(v) With potassium permanganate. An excess of 0·101N-potassium permanganate solution (20 ml.) was added to trifluoromethylphosphonous acid solution (10 ml.) containing an excess of 5N-sulphuric acid (20 ml.). The mixture was heated to 60°, cooled, left for 2 hr., then back-

titrated with 0·0901N-ferrous sulphate (8·07 ml.); 99% of the trifluoromethylphosphonous acid had been oxidised.

The normality of trifluoromethylphosphonous acid for an oxidation titration is twice that for a base titration [cf. $CF_3 \cdot PHO(OH) + O \longrightarrow CF_3 \cdot PO(OH)_2$; $CF_3 \cdot PHO(OH) + NaOH \longrightarrow CF_3PHO(ONa)$].

(d) *Attempted preparation of the anhydrous acid.* Potassium trifluoromethylphosphonite (0·5 g.) heated (60°) with concentrated sulphuric acid (1 ml.) was oxidised to trifluoromethylphosphonic acid; sulphur dioxide was produced.

When potassium trifluoromethylphosphonite (0·5 g.), phosphoric acid (1 g.), and phosphoric anhydride (1 g.) were heated gently with a micro-burner, trifluoromethylphosphine (0·23 g.) (Found: *M*, 101. Calc. for CH_3F_3P: *M*, 102) was the only volatile product.

(e) *Hydrolysis of trifluoromethylphosphonous acid.* A solution of the acid (20 ml. of 0·0655N), heated in a sealed tube at 100° (24 hr.), gave fluoroform (0·0885 g., 97%) and phosphorous acid (98%, by titration with iodine solution).

The hydrolysis in presence of hydriodic acid followed a similar course. Di-iodotrifluoromethylphosphine (2·6 g.) and water (10 ml.) were heated at 140° for 24 hr. to give fluoroform (0·50 g., 98%) and phosphorous acid (0·60 g., 99%).

In a third experiment, di-iodotrifluoromethylphosphine (4·68 g.) and water (5 ml.), heated at 140° (24 hr.) in an 80-ml. tube, gave fluoroform (0·8525 g., 92%), trifluoromethylphosphine (0·0375 g., 8%), and phosphorous acid (0·9716 g., 90%). The volatile products were identified by infrared spectroscopy in the usual way.

Disproportionation of Trifluoromethylphosphonous Acid.—That the acid disproportionates into trifluoromethylphosphine and trifluoromethylphosphonic acid when prepared in concentrated aqueous solution is shown by the following experiments on the hydrolysis of di-iodotrifluoromethylphosphine.

(*a*) The di-iodide (2·6 g., 0·007 mole) and water (4·9 g., 0·27 mole) were kept under a nitrogen atmosphere until the solution was homogeneous (2 hr.). When the liquid was frozen and freeze-dried it was found to be completely volatile, *i.e.*, contained only trifluoromethylphosphonous acid and hydriodic acid.

(*b*) The reaction product from di-iodotrifluoromethylphosphine (5·2 g., 0·015 mole) and water (3·8 g., 0·21 mole) was completely volatile when freeze-dried.

(*c*) Di-iodotrifluoromethylphosphine (25·3 g., 0·071 mole) and water (9·8 g., 0·54 mole) were kept for 12 hr. so that the two layers initially present merged into one. The solution was freeze-dried (14 days) to give trifluoromethylphosphonic acid [3·2 g., 45% of theory expected from the equation $3CF_3 \cdot P(OH)_2 \longrightarrow 2CF_3 \cdot PO(OH)_2 + CF_3 \cdot PH_2$] as a white solid residue, trifluoromethylphosphine (1·01 g., 42% of theory expected from the last equation) (Found: *M*, 103. Calc. for CH_3F_3P: *M*, 102), and a condensate containing trifluoromethylphosphonous acid. The trifluoromethylphosphine was purified by treatment with water (20 ml.) to remove contaminating hydriodic acid, followed by fractionation *in vacuo*; it was identified by means of its infrared spectrum. Trifluoromethylphosphonic acid was purified by sublimation *in vacuo*, leaving no residue, and titration with sodium hydroxide solution revealed two points of inflection and an equivalent weight of 76·5 (Calc. for $CH_3O_3F_3P$: equiv., 75) (cf. Part X). The acid was identified by preparation of its monopotassium salt by reaction of potassium carbonate (0·105 g.) with a solution of the acid (0·23 g.) in water (5 ml.) followed by evaporation to dryness *in vacuo* (Found: K, 20·7. Calc. for CHO_3F_3KP: K, 20·8%). The infrared spectrum was identical with that of known monopotassium trifluoromethylphosphonate. The monoanilinium salt (0·21 g.) was prepared from the acid (0·264 g.), aniline (0·15 g.), and ethanol (1 ml.), and recrystallised from ethanol (Found: C, 34·2; H, 3·3; N, 5·7. Calc. for $C_7H_9O_3NF_3P$: C, 34·5; H, 3·7; N, 5·8%); it had an infrared spectrum identical with that of an authentic sample. Final confirmation was given by the preparation of the dianiline salt from the acid (0·32 g.), aniline (0·45 g.), and ethanol (2 ml.). The salt (0·40 g.) (Found: C, 46·4; H, 4·6; N, 8·2. Calc. for $C_{13}H_{16}O_3N_2F_3P$: C, 46·4; H, 4·8; N, 8·3%) was recrystallised from ethanol, and was spectroscopically identical with known dianilinium trifluoromethylphosphonate. That the trifluoromethylphosphonic acid so prepared was uncontaminated by trifluoromethylphosphonous acid was shown by its failure to liberate fluoroform when treated with 15% sodium hydroxide for 48 hr.

Conductivities in Aqueous Solution.—Solutions were made up by weight, in conductivity water ($\kappa < 1 \times 10^{-6}$), and were diluted by weight. All measurements were made at 25° ± 0·02° in cells of conventional design with sealed-in platinised platinum electrodes. The cells had cell constants 13·29 (A), 4·359 (later 4·347) (B), and 0·05338 (later 0·05112) (C). Resistances

were measured by a Wheatstone bridge circuit with a cathode-ray oscilloscope as null-point detector (Haszeldine and Woolf, *Chem. and Ind.*, 1950, 544). Auxiliary resistances were used in parallel when the cell resistance became greater than 10,000 ohms, and in series when the resistance was less than 500 ohms. In the following Tables, c = concentration (moles/l.), κ = specific conductivity, λ_c = molecular conductivity, $\lambda_{corr.}$ = corrected molecular conductivity, calculated from the equation $\lambda_v = \lambda_{corr.} - (A + B\lambda_{corr.})\sqrt{c}$ with $A = 60{\cdot}21$, $B = 0{\cdot}2289$.

In Table 1, α ($= \lambda_c/\lambda_\infty$) was calculated from the equation $\lambda_x = \lambda_\infty - (A + B\lambda_\infty)\sqrt{c\lambda_c/\lambda_x}$. Provisional values of λ_x were obtained for different concentrations, the quantity λ_x under the square-root sign being replaced by λ_∞. The approximate results for λ_x were then used in the $\sqrt{c\lambda_c/\lambda_x}$ term and a more accurate value of λ_x computed; this was continued until λ_x remained constant, and α was then calculated.

The calculation of ionisation constant K from α cannot lead to accurate values for K, particularly since for strong acids, with $\alpha \sim 1$, a small change in α makes a very large change in K.

(a) *Trifluoromethylphosphonic acid.* This was prepared from the iodotrifluoromethylphosphine (Part X) and was purified by sublimation *in vacuo*. The results are shown in Table 5.

TABLE 5. $CF_3{\cdot}PO(OH)_2$.

10^4c	$10^2\sqrt{c}$	$10^4\kappa$	λ_v	Cell	10^4c	$10^2\sqrt{c}$	$10^4\kappa$	λ_v	Cell
592·3	24·33	206·7	349·1	A	34·35	5·850	12·95	377·1	B
286·6	16·93	102·3	356·6	A	33·47	5·785	12·56	375·3	B
130·2	11·41	47·35	363·6	A	16·26	4·032	6·262	385·1	B
70·25	8·381	26·02	370·5	A	7·394	2·719	2·961	400·4	B
60·27	7·763	22·39	371·5	B					

(b) *Bistrifluoromethylphosphinic acid.* The acid, prepared as described above, was freshly distilled before use, and gave the results shown in Table 6.

TABLE 6. $(CF_3)_2PO{\cdot}OH$.

10^4c	$10^2\sqrt{c}$	$10^4\kappa$	λ_v	$\lambda_{corr.}$	Cell	10^4c	$10^2\sqrt{c}$	$10^4\kappa$	λ_v	$\lambda_{corr.}$	Cell
278·9	16·70	100·9	362·0	386·6	A	42·59	6·525	16·03	376·5	386·3	B
131·9	11·48	48·76	369·6	386·6	A	16·54	4·068	6·277	379·5	385·5	B
113·6	10·65	42·13	370·9	386·8	A	9·757	3·123	3·717	381·0	385·8	B
73·75	8·590	27·51	373·0	386·3	A, B	5·294	2·301	2·624	382·3	385·8	B

λ_∞ (graphical) = 385·7.

(c) *Trifluoromethylphosphonous acid.* Since this acid cannot be isolated in the anhydrous state, a carefully purified aqueous solution (see p. 571) was standardised by pH titration against aqueous sodium hydroxide; dilutions from the standardised solution were made by weight. The results are given in Table 7.

TABLE 7. $CF_3{\cdot}P(OH)_2$.

10^4c	$10^2\sqrt{c}$	$10^4\kappa$	λ_v	Cell	10^4c	$10^2\sqrt{c}$	$10^4\kappa$	λ_v	Cell
351·5	18·75	121·4	345·3	A	24·58	4·958	8·974	365·1	B
165·6	12·86	58·15	351·1	A	13·57	3·684	4·996	368·1	B
99·82	9·996	35·44	355·0	A	11·61	3·408	4·295	369·8	B
68·16	8·254	24·31	357·1	A	4·342	2·084	1·624	373·9	B
54·29	7·367	19·54	359·9	A, B					

λ_∞ (graphical) = 379·0.

(d) *Potassium trifluoromethylphosphonates.* The results are given in Table 8 and 9.

TABLE 8. $CF_3{\cdot}PO(OH)(OK)$.

10^4c	$10^2\sqrt{c}$	$10^4\kappa$	λ_v	Cell
476·4	21·83	51·3	107·6	A
192·1	13·86	22·95	119·5	A
104·7	10·23	13·51	129·0	A, B
58·51	7·650	8·547	146·1	B
48·19	6·940	7·071	145·6	B
29·07	5·392	4·733	162·9	B
15·31	3·912	2·671	174·4	B
11·11	3·333	2·164	194·8	B
4·861	2·205	1·127	231·9	B
2·490	1·578	0·6745	270·9	B

TABLE 9. $CF_3{\cdot}PO(OK)_2$.

10^4c	$10^2\sqrt{c}$	$10^4\kappa$	λ_v	Cell
521·1	22·82	98·45	188·9	B
264·0	16·25	53·01	200·7	B
92·70	9·629	20·12	217·0	B
45·02	6·710	10·29	228·1	B
39·14	6·258	8·973	229·2	B
20·25	4·500	4·807	237·4	B
9·716	3·118	2·377	244·6	B
4·215	2·053	1·065	252·6 *	B
1·933	1·391	0·5052	261·3 *	B

λ_∞ (graphical) = 256·0.

* These points are slightly higher than expected, and may indicate slight hydrolysis of the salt; the second dissociation constant of $CF_3{\cdot}PO(OH)_2$ is $1{\cdot}2 \times 10^{-4}$.

Conductivities in Acetic Acid Solution.—" AnalaR " acetic acid was further purified (Kolthoff and Willman, *J. Amer. Chem. Soc.*, **1934**, **56**, 1007) and had κ 1·5—1·8 × 10^{-8}. The cells and apparatus were the same as used for the aqueous solutions.

The results are given in Tables 10 and 11.

TABLE 10. $CF_3 \cdot PO(OH)_2$ *in acetic acid.*

10^4c	$10^2\sqrt{c}$	$10^8\kappa$	$10^2\lambda_v$	Cell	10^4c	$10^2\sqrt{c}$	$10^8\kappa$	$10^2\lambda_v$	Cell
280·8	16·75	31·48	1·121	C	51·56	7·180	10·50	2·036	C
193·5	13·91	25·26	1·305	C	16·99	4·122	5·641	3·320	C
85·65	9·253	14·40	1·682	C					

TABLE 11. $(CF_3)_2PO \cdot OH$ *in acetic acid.*

10^4c	$10^2\sqrt{c}$	$10^8\kappa$	λ_v	Cell	10^4c	$10^2\sqrt{c}$	$10^8\kappa$	λ_v	Cell
539·2	23·21	25·73	0·4772	C	56·67	7·528	2·883	0·5086	C
308·7	17·57	12·59	0·4079	C	45·40	6·738	2·519	0·5546	C
294·4	17·16	12·69	0·4310	C	25·13	5·013	1·726	0·6869	C
127·6	11·30	5·338	0·4181	C	12·26	3·501	1·177	0·9601	C
111·7	10·57	4·899	0·4385	C					

One of us (R. C. P.) is indebted to the University of Punjab (India) for leave of absence, during which this work was carried out.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 10th*, 1954.]

NOTES.

The Preparation of Tristrifluoromethylphosphine Oxide.

By RAM CHAND PAUL.

[Reprint Order No. 5638.]

TRIMETHYLPHOSPHINE is very readily oxidised to its oxide by exposure to air (Cahours and Hofmann, *Annalen*, **1857**, **104**, 30) whereas trischloromethylphosphine does not react with atmospheric oxygen and yields the oxide only when boiled with nitric acid (Hoffman, *J. Amer. Chem. Soc.*, **1930**, **52**, 2996). Tristrifluoromethylphosphine reacts readily with oxygen but undergoes extensive breakdown and the oxide has not been identified among the products. A further possible method for preparing tristrifluoromethylphosphine oxide is by the aqueous hydrolysis of tristrifluoromethylphosphorus dichloride, but this reaction yields bistrifluoromethylphosphinic acid and fluoroform, while hydrolysis with aqueous alkali gives a salt of trifluoromethylphosphonic acid (Emeléus, Haszeldine, and Paul, *J.*, 1955, preceding paper). It was found, however, that tristrifluoromethylphosphorus dichloride reacted smoothly when heated with an excess of anhydrous oxalic acid according to the equation: $(CF_3)_3PCl_2 + H_2C_2O_4 = (CF_3)_3PO + CO + CO_2 + 2HCl$. Tristrifluoromethylphosphine oxide was produced in a 70% yield. It was a liquid (b. p. 23·5°) and was stable at room temperature. On reaction with water, fluoroform was lost: $(CF_3)_3PO + H_2O = (CF_3)_2PO(OH) + CHF_3$, and with an excess of dilute sodium hydroxide solution 2 mols. of fluoroform were lost and sodium trifluoromethylphosphonate was produced. The reaction with water contrasts with that of alkyl or aryl tertiary phosphine oxides, which form stable hydrates.

Experimental.—Preparation of tristrifluoromethylphosphine oxide. Tristrifluoromethylphosphorus dichloride (5·32 g.) was heated in a 2-necked flask (50 ml.) with anhydrous oxalic acid (2·0 g.; *ca.* 30% excess) over a small flame. The volatile products were swept out of the flask as formed by means of a stream of dry nitrogen. The condenser returned tristrifluoromethylphosphorus dichloride to the flask but a more volatile fraction passed over and was condensed in two traps cooled in liquid oxygen. This condensate was fractionated in the vacuum system and yielded *tristrifluoromethylphosphine oxide* (3·0 g., 70%) (Found: F, 68·1%; *M*, 254. C_3OF_9P requires F, 67·8%; *M*, 254). Vapour pressures, measured with an isoteniscope, gave a b. p. of 23·6°.

Tristrifluoromethylphosphine oxide (0·2343 g.) was sealed in a Carius tube with 10% sodium hydroxide solution (15 ml.) and kept at room temperature for 48 hr. Fractionation of the

volatile products gave fluoroform (0·1285 g.) (Found: *M*, 69·8. Calc. for CHF_3: *M*, 70). The weight of fluoroform expected if two CF_3 groups were removed was 0·1291 g. The solution recovered from the tube was freeze-dried and sodium trifluoromethylphosphonate was identified in the solid residue by means of its infrared spectrum.

Tristrifluoromethylphosphine oxide (0·3918 g.) was sealed in a Carius tube with water (9 ml.) and left for 24 hr. Fractionation of the volatile products gave fluoroform (0·1060 g.), the weight corresponding to the loss of one CF_3 group being 0·1079 g. The solution left in the Carius tube was found to be completely volatile on freeze-drying. It was treated with excess of alkali-free silver oxide (12 hr.) and then filtered. The solution, on freeze-drying, gave silver bistrifluoromethylphosphinate [Found: Ag (as AgCl), 35·1; CF_3 (as CF_3H), 22·1. Calc. for $C_2O_3F_6PAg$: Ag, 35·0; CF_3 (if one CF_3 group is hydrolysed), 22·3%)].

Infrared spectrum of tristrifluoromethylphosphine oxide. The spectrum of this compound (C.S. No. 141)*, recorded on a Perkin-Elmer Model 21 Spectrophotometer, shows strong C–F stretching vibrations at 8·27 and 8·45 μ with overtones at 4·17 and 4·31 μ. The P→O vibration is assigned to the 7·53 μ band by analogy with the spectra of other trifluoromethyl compounds of phosphorus (Bennett, Emeléus, and Haszeldine, *J.*, 1954, 3598), and the CF_3 deformation vibration to the 13·36 μ band.

The author is indebted to the University of Panjab for leave of absence, during which this work was carried out.

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Constituents of the Higher Fungi. Part IV.† *A Quinone from* Polyporus fumosus.

By J. D. Bu'Lock.

[Reprint Order No. 5801.]

Polyporus fumosus (strain number 24A of the Forest Products Research Laboratory collection) grows well on a corn-steep (maize)–glucose medium, and methylene chloride extracts of the culture medium show characteristic strong ultra-violet absorption. From the extracts, a yellow crystalline solid has been isolated. After purification, this had m. p. *ca.* 250° (with sublimation and decomposition); elementary analysis indicated a formula

Absorption spectra (*maxima, in* Å, *followed by* log ε).

3 : 4-Dimethoxy-2 : 5-toluquinone (cf. Vischer, *J.*, 1953, 815) ...	2650 (4·15)	—
2 : 6-Dimethoxybenzoquinone	2860 (4·16)	3800—3830 (2·75)
2 : 5-Dimethoxybenzoquinone (natural and synth.)	2820 (4·13)	3600—3700 (3·53)

$C_8H_8O_4$, with two methoxyl groups. The absorption spectrum (Table) was similar to, but not identical with, that of 2 : 6-dimethoxybenzoquinone, m. p. *ca.* 250° (decomp.), from which it was also distinguished by giving a blood-red, rather than a magenta, colour in concentrated sulphuric acid. The isomeric 2 : 5-dimethoxybenzoquinone was accordingly prepared, and this was found to have the same ultra-violet absorption spectrum and m. p. as, and mixed m. p. with, the natural product. Since criteria of m. p. are inadequate in compounds of this nature, the identification was confirmed by measurements of the infrared spectra (in Nujol mull) of the natural and the synthetic material and of 2 : 6-dimethoxybenzoquinone. The latter compound shows four bands in the region 1500—1700 cm.$^{-1}$ (at 1595, 1620, 1640, and 1690 cm.$^{-1}$), but the more symmetrical 2 : 5-isomer shows only two (at 1660 and 1695 cm.$^{-1}$).

The isolation of 2 : 5-dimethoxybenzoquinone from a natural source has not previously been recorded, but the 2 : 6-isomer was isolated from *Adonis vernalis* (Karrer, *Helv. Chim. Acta*, 1930, **13**, 1424), and then from fermented wheat germ (Vuataz, *ibid.*, 1950, **33**, 433; Cosgrove, Daniels, Whitehead, and Goulden, *J.*, 1952, 4821). In the latter it occurs together with methoxy-1 : 4-benzoquinone, which is known to be formed during the fermentation from a glucoside of the corresponding quinol (de Jong, *Nature*, 1953, **172**, 402). In the present work, corn-steep liquor has been used as a supplement in the culture

* Infrared spectra thus recorded have been deposited with the Society. Photocopies may be obtained, Price 3*s.* 0*d.* per copy, on application to the General Secretary.

† Part III, *J.*, 1953, 3719.

medium, and it is thus possible that the 2 : 5-dimethoxybenzoquinone is similarly formed from a simply related precursor in the liquor. The formation of a substance with a similar absorption spectrum has been observed when other *Polyporus* species were grown on this medium. The third isomer, 2 : 3-dimethoxybenzoquinone, is not known to occur naturally, but the related 2 : 3-dimethoxy-5 : 6-dimethylbenzoquinone is produced, together with the corresponding quinhydrone and β-quinol, by certain *Gliocladium* species (Vischer, *J.*, 1953, 815). In the case of *Polyporus fumosus* (and, apparently, of some other *Polyporus* species which have been examined), preliminary experiments are interpreted as showing that appreciable amounts of the quinone are produced only in the period of relatively rapid growth following inoculation.

Experimental.—The fungus was grown in penicillin flasks on a glucose–salts–corn-steep medium (Hervey, *Bull. Torrey Bot. Club*, 1947, **74**, 476); after 3 weeks, when a full mat of mycelium had formed, the culture medium was drained off and extracted four times with methylene chloride (0·05 pt. by vol.). Evaporation of the combined extracts from 2 l. of medium gave *ca.* 0·1 g. of partly crystalline material. This was purified by vacuum-sublimation or by repeated recrystallisation from ethanol or acetic acid (charcoal). The product, heated on the Kofler block, began to sublime at *ca.* 200° and to melt with decomposition at *ca.* 250° (Found : C, 57·3; H, 5·15; OMe, 38·1. Calc. for $C_8H_8O_4$: C, 57·15; H, 4·8; 2OMe, 37·0%). 2 : 5-Dimethoxybenzoquinone was prepared by the zinc chloride-catalysed addition of methanol to benzoquinone; its behaviour on heating was identical with that of the natural product.

Acknowledgments are made to Professor E. R. H. Jones, F.R.S., for his interest, to the Director of the Forest Products Research Laboratory, Princes Risborough, for the supply of fungus cultures, and to Mr. D. Buckley for a sample of 2 : 6-dimethoxybenzoquinone.

THE UNIVERSITY, MANCHESTER, 13. [*Received, October 13th*, 1954.]

The Reaction between Tellurium and Dichlorodifluoromethane.

By E. E. AYNSLEY and R. H. WATSON.

[Reprint Order No. 5791.]

A RECENT paper (Aynsley, *J.*, 1953, 3016) describes a convenient preparation of tellurium dichloride from dichlorodifluoromethane (Arcton 6) and molten tellurium. A first examination of the gaseous by-products of the reaction showed the presence in them of 1 : 2-dichlorotetrafluoroethane, indicating that the radical $CF_2Cl\cdot$ is involved in the reaction. This communication records a more detailed examination of the products formed at 500°. At this temperature the gaseous by-products contain 1 : 2-dichlorotetrafluoroethane (61·2%), tetrafluoroethylene (16·4%), and 1 : 3-dichlorohexafluoropropane (22·4%). In addition, a minute quantity of a volatile and foul-smelling substance containing tellurium is always formed at 500°, but never in sufficient quantity for identification.

If the radicals $CF_2Cl\cdot$ and $\cdot CF_2\cdot$ are involved then possible reactions which would lead to the by-products are :

$$Te + 2CF_2Cl_2 \longrightarrow TeCl_2 + 2CF_2Cl\cdot$$
$$Te + CF_2Cl_2 \longrightarrow TeCl_2 + \cdot CF_2\cdot$$
$$\cdot CF_2\cdot + CF_2Cl_2 \longrightarrow 2CF_2Cl\cdot$$
$$2CF_2Cl\cdot \longrightarrow C_2F_4Cl_2$$
$$2\cdot CF_2\cdot \longrightarrow C_2F_4$$
$$\cdot CF_2\cdot + CF_2Cl\cdot \longrightarrow CF_2Cl\cdot CF_2\cdot$$
$$CF_2Cl\cdot CF_2\cdot + CF_2Cl\cdot \longrightarrow CF_2Cl\cdot CF_2\cdot CF_2Cl$$

It is clear that the first reaction would explain the formation of $C_2F_4Cl_2$ but not that of the other two compounds, whereas if the second reaction is assumed to constitute the initiation then the presence of all three compounds can be accounted for. Moreover the reaction $CF_2Cl\cdot + CF_2Cl_2 \longrightarrow CF_3Cl + CFCl_2\cdot$ does not occur under these conditions since chlorotrifluoromethane was not found among the products.

An alternative scheme for the formation of tetrafluoroethylene and the $CF_2Cl{\cdot}CF_2{\cdot}$ radical is:

$$Te + 2C_2F_4Cl_2 \longrightarrow TeCl_2 + 2CF_2Cl{\cdot}CF_2{\cdot}$$
$$Te + C_2F_4Cl_2 \longrightarrow TeCl_2 + C_2F_4$$
$$Te + 2CF_2Cl{\cdot}CF_2{\cdot} \longrightarrow TeCl_2 + C_2F_4$$

This avoids the assumption of the $\cdot CF_2\cdot$ radical but requires the further reaction of initial products with the tellurium. In the flow method used the chances of this are small. The further possibility that tetrafluoroethylene is formed by the pyrolysis of the dichloride is unlikely since the time spent by the vapours in the hot zone was short (~15 sec.). Furthermore the chlorine liberated would be likely to convert some tellurium dichloride into the tetrachloride, and this was absent from the solid product. It thus seems that the scheme involving $\cdot CF_2\cdot$ radicals is the more probable.

Not more than 0·2% of perfluoro*cyclo*butane was formed, this being the limit of detection in our process. Further the total weight of chlorine in the tellurium dichloride and in the three by-products equalled that lost by the dichlorodifluoromethane. The $C_3F_6Cl_2$ fraction, b. p. 35·5°, could be 1 : 2- or 1 : 3-dichlorohexafluoropropane, which are practically indistinguishable by boiling point, density, or refractive index. It is known that tetrafluoroethylene dimerises at 500° but that the formation of hexafluoropropylene, occurs only at higher temperatures (Atkinson and Trenwith, *J.*, 1953, 2082). Since this is the only likely compound from which the 1 : 2-dichloro-compound could be formed in our preparation, we have assumed that the $C_3F_6Cl_2$ is, in fact, the 1 : 3-dichloro-compound.

Experimental.—Arcton 6 (from Imperial Chemical Industries Limited), washed with potassium hydroxide solution and dried with concentrated sulphuric acid and with phosphoric oxide, was led over molten tellurium at 500° contained in the first section of a 25-mm. Pyrex tube, constricted at intervals of about 10 cm. to furnish six compartments. The tellurium dichloride was distilled forward in the gas stream from section to section and finally into a receiver. Beyond this was a 10-cm. tube containing glass wool and "Carbosorb" to remove small amounts of tellurium compounds carried forward in the gas stream. The unchanged Arcton 6 together with the gaseous by-products of the reaction then passed into a trap surrounded by liquid air. This trap was protected by a drying tube and a potassium hydroxide tube.

Fraction	B. p.	*M* (calc.)	*M* (obs.)	Vol. % in distn. mixture	Vol. % of gaseous by-products	Weight (g.)
C_2F_4	−76·3°	100	100·6 ± 1·0	1·40	16·4	0·0876
CF_2Cl_2 (un-decomp.)	−30·0	121	—	91·44	—	6·9296
$C_2F_4Cl_2$	+ 3·6	171	170·3 ± 1·0	5·24	61·2	0·5617
$C_3F_6Cl_2$	+35·5	221	222·0 ± 3·0	1·92	22·4	0·2662

The contents of the trap were transferred to the bottom of a Podbielniak-type low-temperature fractionation column (Podbielniak, *Ind. Eng. Chem.*, 1931, **3**, 177), and the amounts and molecular weights of the fractions were determined (see Table). Because the separation of the fractions was sharp, the apparatus was capable of detecting 1 pt. of a compound in 500 pt. of total material. 1·4750 g. of tellurium dichloride was collected, and the weight of chlorine in this together with the weights of carbon, fluorine, and chlorine in the by-products gave a C : F : Cl ratio of 1 : 2 : 2.

KING'S COLLEGE, NEWCASTLE-ON-TYNE, 1. [*Received, October 9th*, 1954.]

Synthesis of Plant-growth Regulators. Part IV. Substituted α-2-Naphthyloxypropionic Acids.*

By (MRS.) P. M. POPE and D. WOODCOCK.

[Reprint Order No. 5790.]

SUBSTITUTED β-naphthyloxyacetic acids (James and Woodcock, *J.*, 1951, 3418; 1953, 2089) have been examined for parthenocarpic activity, by using unpollinated tomato ovaries, and the effect of the position of the nuclear chlorine atoms on the activity of the molecule has been shown to be critical (Luckwill and Woodcock, unpublished). α-2-Naphthyloxy-

* Part III, *J.*, 1954, 1721.

propionic acid has recently been found to be as effective as the corresponding acetic acid as a fruit-setting spray for outdoor tomatoes (Wain, *J. Hort. Sci.*, 1950, **25**, 249). Substituted α-2-naphthyloxypropionic acids, prepared for a similar investigation, are now described. Other members of this and similar series have already been tested for systemic fungicidal activity against chocolate spot of broad bean caused by *Botrytis fabae* (Byrde, Crowdy, and Woodcock, *Ann. Appl. Biol.*, 1953, **40**, 152).

Differences in the plant-growth regulating activity of optical isomers have been reported by several workers. Thus Kögl and Verkaaik (*Z. physiol. Chem.*, 1944, **280**, 167) found that (+)-α-3-indolylpropionic acid was some thirty times more active than the (−)-form in the Avena curvature test, and Smith and Wain (*Proc. Roy. Soc.*, 1951, *B*, **139**, 118) have shown that (+)-α-2-naphthyloxypropionic acid is similarly highly active in six different tests, whereas the (−)-form has little or no activity. Resolution of (±)-α-(3-chloro-2-naphthyloxy)propionic acid with cinchonine is described in the present paper. This acid provides yet another example of a racemic plant-growth substance providing a highly active (+)-form and a correspondingly inactive (−)-form on resolution.

Experimental.—α-2-Naphthyloxypropionic acid. The product, m. p. 114—115°, obtained on several occasions is interconvertible with that previously recorded by Bischoff (*Ber.*, 1900, **33**, 1390) as of m. p. 107—108°, and is probably identical with the modification reported by Fregda and Matell (*Arkiv Kemi*, 1951, **3**, 429). We are grateful to a referee for drawing our attention to the later paper. Each of the above forms gave the same *amide* and S-*benzylthiuronium salt*. The amide formed small rectangular prisms, m. p. 157—157·5°, from benzene (Found: C, 72·5; H, 6·0; N, 6·5. $C_{13}H_{13}O_2N$ requires C, 72·6; H, 6·0; N, 6·5%). Fourneau and Balaceano (*Bull. Soc. chim.*, 1925, **37**, 1602) give m. p. 169° but no analytical results. The salt, prepared in aqueous solution, crystallised from 50% aqueous ethanol in rhombs, m. p. 159—159·5° (Found: C, 65·8; H, 5·7; N, 7·3; S, 8·2. $C_{21}H_{22}O_2N_2S$ requires C, 66·0; H, 5·8; N, 7·3; S, 8·4%).

Substituted α-2-naphthyloxypropionic acids. These were prepared by condensation of ethyl α-bromopropionate and the sodium salt of the appropriate naphthol, as described for the corresponding acetic acids in Part I, analytical details being tabulated below. Crystallisation from methanol or ethanol alone was avoided since esterification was rapid in hot solution. Thus, on one occasion *methyl α-(3-chloro-2-naphthyloxy)propionate* was isolated from the mother liquors, as large rhombs, m. p. 77—78° (Found: C, 63·4; H, 4·9; Cl, 13·5. $C_{13}H_{11}O_3Cl$ requires C, 63·5; H, 4·9; Cl, 13·4%).

Resolution of α-(3-chloro-2-naphthyloxy)propionic acid. A solution of the (±)-acid (5·0 g.) and cinchonine (5·8 g.) in boiling methanol (50 ml.) was diluted with hot water and allowed to cool. The *cinchonine salt* of the (−)-acid, which gradually separated, was twice recrystallised from aqueous methyl alcohol; monoclinic prismatic plates, which decomposed at 148—150° after softening *ca.* 125°, were obtained (Found: C, 68·2; H, 6·2; loss in vacuum at 110°, 3·2. $C_{13}H_{11}O_3Cl,C_{19}H_{22}ON_2,H_2O$ requires C, 68·2; H, 6·2; loss 3·2%); $[\alpha]_D^{21}$ +33·2° (*c*, 1·022 in MeOH). Concentration of the mother liquors yielded a little more of the same salt, and

Substituted α-2-naphthyloxypropionic acids, $RR'C_{10}H_6{\cdot}O{\cdot}CH(Me{\cdot})CO_2H$.

		Found, %				Required, %		
RR′	M. p.	C	H	Cl or N	Formula	C	H	Cl or N
3-Cl,H	175—176°	62·1	4·4	14·1	$C_{13}H_{11}O_3Cl$	62·3	4·4	14·2
4-Cl,H	123—124	62·3	4·3	14·2	,,	,,	,,	,,
5-Cl,H	173—174	62·2	4·4	14·2	,,	,,	,,	,,
6-Cl,H	157—158	62·3	4·2	14·1	,,	,,	,,	,,
8-Cl,H	132—133	62·3	4·2	14·2	,,	,,	,,	,,
5 : 6-Cl_2	148—149	55·0	3·4	24·8	$C_{13}H_{10}O_3Cl_2$	54·8	3·5	24·9
5-NO_2,H	200—201	60·5	4·3	N, 5·1	$C_{13}H_{11}O_5N$	59·8	4·2	5·4
8-NO_2,H	183—184	59·8	4·4	N, 5·0	,,	,,	,,	,,

Solvent: aqueous methanol for the chloro-compounds, aqueous acetic acid for the nitro-compounds.

eventually the cinchonine salt of the (+)-acid was obtained as a gum. The two salts were separately dissolved in chloroform, the solutions shaken with dilute ammonia solution, and the acids recovered from the alkaline layers were crystallised twice from aqueous methanol. The (−)-*acid*, obtained as a matte of fine needles, m. p. 175—176° (Found: C, 62·5; H, 4·4; Cl, 13·8. $C_{13}H_{11}O_3Cl$ requires C, 62·3; H, 4·4; Cl, 14·2%), had $[\alpha]_D^{21}$ −56·8° (*c*, 1·012 in MeOH). The (+)-*acid* crystallised in fine needles, m. p. 175—176°, $[\alpha]_D^{20}$ +55·6° (*c*, 0·990 in MeOH)

(Found: C, 62·3; H, 4·4; Cl, 14·1%). Crystallisation of equimolecular proportions of the (+)- and the (−)-acid from aqueous methanol yielded the (±)-acid, m. p. 175—176°.

The authors thank Mr. J. F. Harris for the analytical results.

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Oxidation of Some Enediols with Selenium Dioxide.

By J. R. HOLKER.

[Reprint Order No. 5710.]

COMPOUNDS of the type HO·CR:CR'·OH are generally readily oxidised to R·CO·CO·R' with, *e.g.*, iodine, Tillmann's reagent (2 : 6-dichlorophenol–indophenol), and silver oxide. The first two reagents can be applied to the quantitative estimation of the enediol group (see, *e.g.*, von Euler, " Sammlung chemischer und chemisch-technischer Vorträge," Enke, Stuttgart, 1950, Heft 50), but are not always suitable for preparatory work. Silver oxide and other reagents are usually satisfactory only when the product is stable to further oxidation.

We have found that a number of enediols possessing an α-carbonyl group are rapidly and quantitatively oxidised in aqueous or alcoholic solution by selenium dioxide. The reaction is slightly exothermic. After removal of precipitated selenium, recovery of the oxidation product is extremely simple.

Mesoxaldehyde was obtained from reductone, and use of excess of selenium dioxide did not cause further oxidation to mesoxalic acid. The preparation of crystalline dehydro-L-ascorbic acid requires anhydrous conditions, and by using chlorine in dry methanol, Pecherer (*J. Amer. Chem. Soc.*, 1951, **73**, 3827) obtained a 39% yield; oxidation with selenium dioxide in anhydrous ethanol readily afforded a high yield of the crystalline dehydro-acid. Svirbely (*Biochem. J.*, 1938, **32**, 467) observed a low content of ascorbic acid in the organs of selenite-poisoned rats. Dihydroxymaleic acid in aqueous solution gave dihydroxytartaric acid, isolated as the sparingly soluble sodium salt. The deep red reduced form of perinaphthindanetrione is rapidly re-oxidised to the trione in alcoholic solution. The reaction will be extended to other enediols as these become available from another investigation.

This reaction has been extended to the use of selenium dioxide as a spray for paper chromatograms of reductone. Reddish-brown spots of selenium are produced in the cold and their stability to light and air make the reagent more suitable than silver nitrate or Tillmann's reagent. Aqueous solutions of reductone slowly decompose. Paper chromatograms of such solutions gave no other spot with selenium dioxide, indicating that the decomposition products are not enediols.

Experimental.—Mesoxaldehyde. Reductone (Cocker *et al.*, *J.*, 1950, 2052) was rapidly recrystallised from water (60°), with considerable loss, and dried (P_2O_5). This material [1·0 g.; m. p. 149° (decomp.)] in water (10 ml.) was shaken for 1 hr. with selenium dioxide (0·6 g.) in water (10 ml.). The mixture was kept overnight, selenium (0·45 g.) filtered off, and the filtrate treated with aqueous phenylhydrazine acetate. The precipitated mesoxaldehyde bisphenylhydrazone had m. p. 174—175° after recrystallisation. Moubasher (*J. Biol. Chem.*, 1948, **176**, 532) gives m. p. 176°.

Use of a large excess (2·0 g.) of selenium dioxide gave only 0·48 g. of selenium.

Dehydro-L-ascorbic acid. Dried selenium dioxide (0·55 g.) (1 hr. at 100°) was shaken for 1 hr. with L-ascorbic acid (1·74 g.) in freshly purified ethanol (20 ml.); the acid slowly dissolved and selenium was precipitated. The following day the solution, after removal of selenium (96%) by filtration, was evaporated and finally heated to 100° *in vacuo*. The syrup slowly yielded a semisolid which solidified completely when boiled with a few ml. of xylene. The powder had m. p. 222—224° (decomp.); Pecherer (*loc. cit.*) gives m. p. 220—225° (decomp.). It gave the bright orange 2 : 4-dinitrophenylosazone, m. p. 274—275°; Penney and Zilva (*Biochem. J.*, 1943, **37**, 404) give m. p. 280°. An aqueous solution of the dehydro-acid exhibited typical mutarotation; it also gave the characteristic pink colour, deepening with heat, with glycine (Pecherer, *loc. cit.*).

Oxidation was also carried out in methanol. The syrup produced crystallised when boiled with xylene for a few minutes.

Dihydroxytartaric acid. Selenium dioxide (0·6 g.) in water (20 ml.) was shaken with dihydroxymaleic acid (1·5 g.) for 2 hr. Selenium was filtered off and the filtrate neutralised with 10% sodium hydroxide solution. After 2 hr. at 0°, the insoluble sodium dihydroxytartrate was filtered off, washed, and dried (P_2O_5); the yield was 0·75 g. It gave diketosuccinic acid osazone, m. p. 200—201° (decomp.); Moubasher (*loc. cit.*) gives m. p. 200°. When this oxidation was carried out in 95% ethanol the product was an oil which did not crystallise after several days at 0°.

Perinaphthindanetrione. This was obtained from the reduced form (dihydroxyperinaphthindenone) in alcohol solution. After crystallisation from water it had m. p. and mixed m. p. 267—269° (decomp.).

Paper chromatography of reductone. Freshly prepared aqueous reductone (2·5%; 0·005 ml.) was chromatographed on Whatman No. 1 paper for 16 hr., the upper phase of a *n*-butanol–acetic acid–water mixture (100 : 20 : 50 v/v) being used. After being roughly dried at room temperature for 30 min. the paper was sprayed with 1% selenium dioxide solution. A red-brown spot (R_F 0·58—0·59) appeared immediately. Weygand (*Arkiv Kemi*, 1951, **3**, 11) gives reductone R_F 0·59—0·64. The same reductone solution, after 48 hours in a stoppered tube gave only one weak spot with selenium dioxide (R_F 0·58).

The author thanks the International Wool Secretariat for the award of a Research Fellowship.

Department of Textile Industries, The University, Leeds, 2. [*Received, September 17th*, 1954.]

Quantitative Analysis of Mixtures of Sodium, Potassium, Magnesium, and Calcium by Paper Chromatography.

By D. R. Tristram and C. S. G. Phillips.

[Reprint Order No. 5684.]

For a number of purposes, especially the characterisation of certain minerals, a simple method is required for the estimation of sodium, potassium, calcium, and magnesium, in the form of their chlorides, in the presence of one another and of hydrochloric acid, and with an accuracy of 2—3%. This paper describes how such analyses may be effected by means of paper chromatography. After the chromatography, the chloride bands are converted on the paper into the equivalent amount of metallic silver. For quantitative analysis the silver bands are dissolved in nitric acid, and the silver titrated with ammonium thiocyanate. The method is suitable for 100 μg. to 10 mg. of the salts.

Experimental

Chromatography.—The separation of the alkali metals and of the alkaline earths on cellulose as chlorides was first described by Burstall, Davies, Linstead, and Wells (*J.*, 1950, 516). We have found Whatman 540 (supplied in strips) the best paper. It gives a low background and retains its strength when wet. The best solvent found was laboratory ethyl alcohol containing an additional 6% of water. The solution to be analysed is run on to the strips from a microburette, by stroking the tip of the burette across the strip about 2 in. from the end. The strip is then dried for a few minutes, and placed in the normal paper chromatography apparatus. After chromatography for 12—20 hr. the strips are removed and the alcohol allowed to evaporate. The strip is dipped into 0·1N-silver nitrate, which causes all the chloride ion to be precipitated on the strip as silver chloride. The strip is then thoroughly washed with distilled water, soaked in a bath of photographic developer to reduce the silver chloride to metal, and finally washed again. At this stage the bands show up very clearly and enable a rough quantitative analysis to be made by inspection.

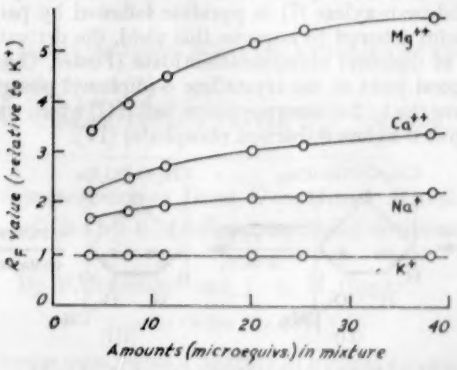
Quantitative Determination.—The silver bands are cut out and placed separately in small (2″) evaporating dishes. 2N-Nitric acid (5 ml.) is then added to each dish, and they are warmed until the bands are decolorised. When cool, crystals of ferric nitrate are added, and the solutions titrated with 0·1N-ammonium thiocyanate from a microburette (capacity 0·1 ml.) calibrated in thousandths of a ml. The paper remains in the dishes during the titrations.

Results and Discussion

Accuracy.—The accuracy of the conversion and titration procedure, tested by carrying out the above operations without any chromatography, is 1—2%. The overall accuracy thus depends upon the chromatography, the two main sources of error being the paper and incomplete separation. Traces of calcium, magnesium, and other metals on the paper give rise to diffuse bands. Anything which reacts with silver nitrate produces a background. For these reasons ordinary filter paper is not satisfactory. Incomplete separation of the sodium and the calcium bands occurs when insufficient time is allowed for the chromatography. Good results are obtained after 12—20 hours, the solvent front then having passed off the end of the paper.

The Table gives results of four runs on solutions made up by the senior and analysed by the junior author. The values quoted are in microequivalents (ml. of 0·1N-ammonium thiocyanate × 100).

	K	Na	Ca	Mg		K	Na	Ca	Mg
	Mixture A.					*Mixture C.*			
Correct	20·0	20·0	20·0	20·0	Correct	22·8	17·1	28·6	11·4
Estimated	18·5	19·0	20·0	20·8	Estimated	20·6	16·3	27·6	12·7
Error (% of total) ...	−2	−1·2	0	+1	Error (% of total) ...	−2·8	−1	−1·3	+1·6
	Mixture B.					*Mixture D.*			
Correct	14·5	14·5	35·5	14·5	Correct	16·0	8·0	16·0	4 ·0
Estimated	13·9	14·3	34·9	15·3	Estimated	15·0	8·7	14·6	38·4
Error (% of total) ...	−0·8	−0·3	−0·8	+1	Error (% of total) ...	−1·3	+0·9	−1·8	−2



Hydrochloric Acid.—The presence of hydrochloric acid in concentrations of the same order as the metal ions leads to no appreciable error. The acid is carried down near the solvent front and runs off the end of the strip. This is an attractive feature of the method, if, for example, a dolomite has been brought into solution with hydrochloric acid.

Ammonium, Lithium, Barium, and Strontium.—Excellent separations of potassium, sodium, ammonium, and lithium, and of barium, strontium, and calcium have been obtained by the same methods, and we have made quantitative analyses of mixtures of potassium, sodium, calcium, magnesium, and lithium. In each of these mixtures the bands appear in the order written.

Displacement.—The fact that sodium and calcium are satisfactorily separated suggests that they must possess very different R_F values. However, when the two ions are run separately there is little difference in R_F value. This seems to indicate that displacement is involved in the early stages of the separations. The effect may also be illustrated by the results in the Figure, in which the R_F values of sodium, calcium, and magnesium (relative to potassium) increase up to a limit with the concentration of the sample on the strip.

Inorganic Chemistry Laboratory, Oxford. [*Received, August 26th*, 1954.]

Addendum: Chemical Action of Ionizing Radiations in Aqueous Solutions. Part XIII. Absolute Yield of the Ferrous Sulphate Dosimeter.*

By F. T. Farmer, T. Rigg, and J. Weiss.

[Reprint Order No. 5819.]

Since the paper under the above title was submitted the National Physical Laboratory have made known (Wyckoff, Aston, and Smith, *Brit. J. Radiol.*, **1954**, **27**, 325) that their standardisation of dosimeters is subject to a further correction of about 4% in the same direction as the 3% already referred to in our paper. This will further reduce the value of G from **16·2** there quoted, and will bring the yield of the ferrous ⟶ ferric reaction for X-rays (200 kv) to $G = 15{\cdot}6 \pm 0{\cdot}8$ moles per **100** ev.

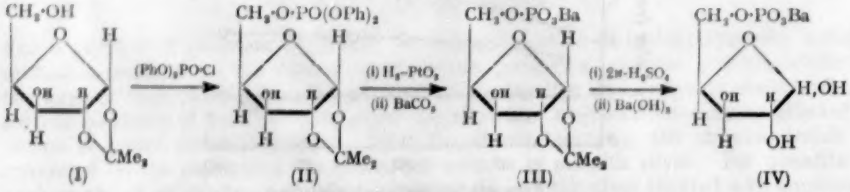
King's College, Newcastle-on-Tyne, 1. [*Received, October 25th*, 1954.]

An Improved Synthesis of D-*Xylose* 5-(*Barium Phosphate*).

By P. A. J. Gorin, L. Hough, and J. K. N. Jones.

[Reprint Order No. 5772.]

D-Xylose 5-(barium phosphate) was synthesised by Levene and Raymond (*J. Biol. Chem.*, 1933, **102**, 347) in rather low yield (16—18%) by the reaction of phosphorus oxychloride with 1 : 2-*O*-*iso*propylidene-D-xylose (I) in pyridine followed by partial hydrolysis of the product. In a successful attempt to improve this yield, the derivative (I) was treated in pyridine with 1 mol. of diphenyl phosphorochloridate (Foster, Overend, and Stacey, *J.*, 1951, 980) to give a good yield of the crystalline 5-(diphenyl phosphate) (II). Catalytic hydrogenation then gave the 1 : 2-*O*-*iso*propylidene salt (III) which was partially hydrolysed with mineral acid to give D-xylose 5-(barium phosphate) (IV).



Like triphenylmethyl chloride and other activated chlorides, diphenyl phosphorochloridate reacts preferentially with the primary alcohol group giving, in this case, the 5- and not the 3-phosphate. The resistance of the phosphate ester (IV) to conditions of acid hydrolysis that would completely hydrolyse a 3-phosphate of xylose (Levene and Raymond, *J. Biol. Chem.*, **1934**, **107**, 75) confirms the structure of the product.

It is interesting that the *iso*propylidene group in (III) is remarkably stable to acid hydrolysis, requiring 2N-sulphuric acid at 100° for 3 hours for complete removal. This stability is clearly attributable to the presence of the phosphate group, since in its absence, the *iso*propylidene group can be removed by 0·01N-sulphuric acid at 100° in 1 hour.

Experimental.—Determinations of carbon and hydrogen are by Mr. B. S. Noyes of Bristol.

1 : 2-O-iso*Propylidene*-D-*xylose* 5-(*diphenyl phosphate*) (II). Diphenyl phosphorochloridate (2·5 g.; 1·1 mol.) was added to 1 : 2-*O*-*iso*propylidene-D-xylose (1·74 g.) in dry ice-cold redistilled pyridine (3 c.c.). After 10 min. at 0° the solution was set aside at room temperature for 1 hr., then shaken with chloroform (25 c.c.) and aqueous sodium hydrogen carbonate (25 c.c.); the chloroform layer was separated, washed with water, dried ($MgSO_4$), filtered, and evaporated to a syrup (3·39 g.) which crystallised. Recrystallisation from light petroleum (b. p. 60—80°) gave the *ester* as needles, m. p. 99—100°, $[\alpha]_D^{20}$ +3° (*c*, 1·48 in $CHCl_3$) (Found: C, 56·7; H, 5·6; P, 7·6. $C_{20}H_{23}O_8P$ requires C, 56·9; H, 5·5; P, 7·3%).

* See *J.*, 1954, 3248.

1 : 2-O-iso*Propylidene*-D-*xylose* 5-(*barium phosphate*) (III). A solution of the ester (II) (810 mg.) in 32% aqueous methanol (66 c.c.) containing Adams platinic oxide (75 mg.) was shaken in hydrogen at slightly more than 1 atm. After 8 hr., when uptake of hydrogen had ceased, the catalyst was filtered off and the solution neutralised with barium carbonate. Insoluble material was filtered off and the filtrate evaporated under reduced pressure to a white solid (610 mg.), $[\alpha]_D^{20}$ −2·5° (*c*, 3·0 in MeOH).

D-*Xylose* 5-(*barium phosphate*) (IV). The *iso*propylidene salt (434 mg.) in 2N-sulphuric acid (8 c.c.) was heated at 100° for 3 hr. The solution was adjusted to pH 8 by aqueous barium hydroxide solution and filtered. The precipitate was washed and the filtrate evaporated under reduced pressure to a small volume. Paper chromatography showed the presence of unchanged (III) and xylose in addition to (IV). An excess of acetone was added to the aqueous solution, and the precipitate filtered and then triturated with a little ethanol to remove traces of impurities. The product [220 mg.; 47% overall yield from (I)] had $[\alpha]_D^{20}$ +8° (*c*, 0·85 in H_2O) [Found : C, 19·9; H, 3·2. Calc. for $(C_5H_{10}O_8P)_2Ba$: C, 20·2; H, 3·4%]. Levene and Raymond (*loc. cit.*, 1933) record $[\alpha]_D^{22}$ +5° (*c*, 2·0 in H_2O). It gave on paper chromatograms (Whatman No. 542 filter paper; ethyl acetate–acetic acid–formic acid–water, 18 : 3 : 1 : 4 v/v) one discrete spot (rate 0·3 relative to galactose) which was pink with the *p*-anisidine hydrochloride spray (Hough, Jones, and Wadman, *J.*, 1950, 1702) and blue with the ammonium molybdate–perchloric acid–phosphate spray (Hanes and Isherwood, *Nature*, 1949, **164**, 1107).

To a solution of D-xylose 5-(barium phosphate) (40·32 mg.) in water (25 c.c.) was added 6·13N-sulphuric acid (5 c.c.), the precipitate filtered off, and the filtrate heated at 100°. The liberation of inorganic phosphate was followed by the method of Foster, Overend, and Stacey (*J.*, 1951, 987); 50% hydrolysis was observed after 270 min. This result is similar to that observed by Levene and Raymond (*loc. cit.*, 1934) when they hydrolysed their product with N-hydrochloric acid.

One of us (P. A. J. G.) thanks the Bristol Education Authorities for a grant.

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The Isolation of Oligosaccharides from Gums and Mucilages. Part IV. The Isolation of* 3-O-β-L-*Arabopyranosyl*-L-*arabinose from Lemon Gum.*

By P. ANDREWS and J. K. N. JONES.

[Reprint Order No. 5774.]

PARTIAL hydrolysis of lemon gum yields a mixture of neutral and acidic mono- and oligosaccharides. So far L-arabinose, D-galactose, D-glucuronic acid, a compound that was probably 4-(4-*O*-methyl-D-glucuronopyranosyl)-D-galactose (Connel, Hainsworth, Hirst, and Jones, *J.*, 1950, 1696), and 4-(4-*O*-methyl-α-D-glucuronopyranosyl)-L-arabinose have been separated and characterised (Andrews and Jones, *J.*, 1954, 1724). This publication records the isolation from lemon gum of 3-*O*-β-L-arabopyranosyl-L-arabinose, which was identified by its rate of movement on the paper chromatogram, by its high positive optical rotation, and by the fact that its phenylosazone was indistinguishable by *X*-ray diffraction analysis from the osazone of an authentic specimen of the disaccharide prepared from larch ε-galactan (Jones, *J.*, 1953, 1672). This arabopyranose-containing disaccharide is thus a constituent of larch ε-galactan, peach gum, cherry gum (Andrews, Ball, and Jones, *J.*, 1953, 4090), golden apple gum, and lemon gum. It is also present in the oligosaccharides produced when some commercial samples of gum acacia are hydrolysed but not in those from gum ghatti (unpublished results).

When arabinose is kept in 6N-hydrochloric acid for some days condensation occurs, giving a complex mixture of di- and oligo-saccharides in about 10% yield. Lemon gum on autohydrolysis yields, first, a mixture of arabinose and a neutral pentose-containing disaccharide, 3-*O*-β-L-arabopyranosyl-L-arabinose. On prolonged autohydrolysis the

* Part III, *J.*, 1954, 4134.

latter sugar disappears because it is hydrolysed to arabinose. Similar results are observed when lemon gum is hydrolysed with cold dilute hydrochloric acid. However, when arabinose undergoes reversion in the presence of an acid catalyst, the concentration of di- and oligo-saccharides increases until an equilibrium mixture is reached. It is inferred that the neutral arabinose-containing disaccharide isolated from lemon gum is a true component of the polysaccharide and that it is not an artefact produced by reversion. Nevertheless when the hydrolysis of gums or mucilages is carried out in concentrated solution in the presence of hydrochloric or sulphuric acid, reversion products may be formed in considerable quantity and their isolation may lead to incorrect conclusions as to structure. Further details will be published later.

Experimental

Chromatographic separations were carried out on Whatman No. 1 paper with (*a*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4), and (*b*) *n*-butanol–pyridine–water (10 : 3 : 3). *p*-Anisidine hydrochloride was used as spray. Optical rotations were determined at 20° ± 2° in H_2O. Evaporation of solutions was carried out under reduced pressure.

Hydrolysis of Lemon Gum with Cold Dilute Sulphuric Acid.—Lemon gum (15 g.) was dissolved in cold N-sulphuric acid (150 c.c.), and the solution set aside at 20° ± 5°. Samples were examined at intervals on the paper chromatogram. After 24 weeks (cf. Andrews and Jones, *J.*, 1954, 1724) the solution was brought to pH 5 with barium hydroxide, concentrated to 40 c.c., and poured into alcohol. The precipitated barium salt of the degraded gum was collected, dried, and exhaustively extracted with methanol. The filtrate and alcoholic extracts were combined and evaporated to a syrupy mixture (6·5 g.). A portion (6·0 g.) of this was fractionated on a column of cellulose with ethyl acetate–acetic acid–water (9 : 2 : 2 v/v) as eluant. Those fractions of the effluent containing arabinose and galactose were discarded. Those containing the disaccharide, which was chromatographically pure, were combined and the solvent was evaporated. There remained a syrupy sugar which was purified by dissolution in water and filtration through a bed of charcoal. The solvent was removed from the filtrate and the residual syrup (98 mg.) examined chromatographically. It appeared homogeneous in solvents (*a*) and (*b*), and was indistinguishable from 3-*O*-β-L-arabopyranosyl-L-arabinose, prepared from cherry gum and larch ε-galactan. Its rate of movement relative to sucrose was 1·5 in solvent (*a*) and 1·0 in solvent (*b*), and it had $[\alpha]_D$ +196° ± 10° (*c*, 4·2). On acidic hydrolysis arabinose was the only sugar detectable on the chromatogram. Warming it with phenylhydrazine acetate solution gave an osazone in good yield, having m. p. 240° (block) after recrystallisation from aqueous alcohol (Found: C, 57·1; H, 6·1; N, 12·4. Calc. for $C_{22}H_{28}O_7N_4$: C, 57·4; H, 6·1; N, 12·2%). Its m. p., which depends upon the rate of heating, was not depressed on admixture with an authentic sample. The *X*-ray diffraction pictures of this osazone and of an authentic sample were identical.

Autohydrolysis of the Gum.—Ash-free lemon gum (1·27 g.) was heated in water (10 c.c.) at 90°. At intervals samples were examined on the paper chromatogram. After 12 hours' heating arabinose and a trace of a pentose-containing disaccharide were detected. Thereafter the concentration of arabinose and the disaccharide increased until after 48 hr. the concentration of disaccharide appeared to reach a maximum, and at about this time galactose was detected on the chromatogram. After 60 hr. the galactose and arabinose concentrations had increased considerably while that of the disaccharide had diminished. At this stage the cooled solution was poured into alcohol, the precipitate of degraded gum filtered off, and the alcoholic solution evaporated to a syrup. Chromatography of this syrup (solvent *b*) indicated the presence of arabinose, galactose, and 3-*O*-β-L-arabopyranosyl-L-arabinose. When solvent (*a*) was used additional spots corresponding to the presence of acidic disaccharides appeared.

The authors thank Professor J. E. Hawley, F.R.S.C., for permission to use his *X*-ray equipment. One of them (P. A.) thanks the Directors of Monsanto Chemicals Ltd. for the award of a Fellowship.

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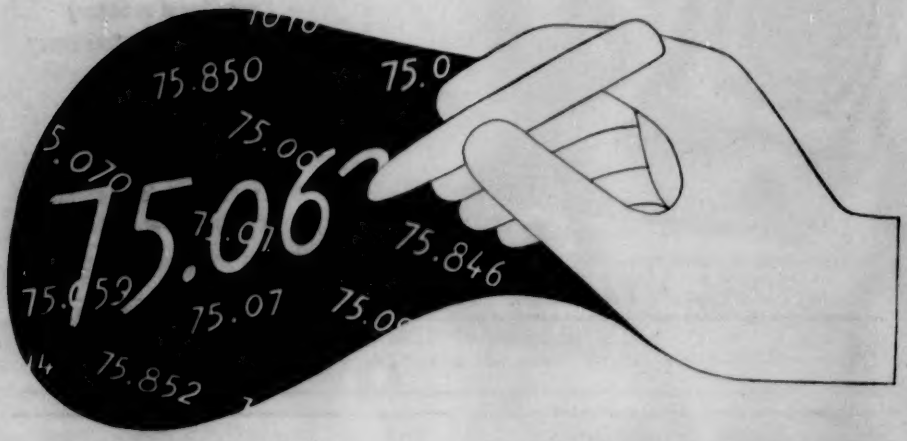

DR. MARCHAND OF BERLIN made this statement in a letter recorded in the first volume of the Proceedings of the Chemical Society (1841), challenging the claim of Liebig and Redtenbacher to have established 75.854 as the correct atomic weight for carbon. In those days atomic weights were related to oxygen as 100, and it is notable that the 1951 atomic weight for carbon calculated on this basis is 75.063 compared with Marchand's figure of 75.07 derived from the combustion of diamond and graphite.

Dr. Marchand, whose methods were simple and direct, would have welcomed the convenience and accuracy of 'AnalaR' reagents. It is even possible that they would have assisted the highly elaborate analytical work of Liebig and Redtenbacher to a more successful result.

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